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Psychiatry

The Newer Drugs in Psychiatric Practice

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In attempting to bring together some of the data about drugs which recently have made their debut, I go back to the wisdom of one of your great clinicians of yesteryear, Sir William Osler, who was an exceedingly astute observer of the medical scene. He left behind many pithy comments or aphorisms about medical practice and is quoted as saying, as he reached for the definition of a drug, "A drug is a substance which, given to a certain number of patients, produces a paper." Although Osler lived in a period characterized by therapeutic nihilism with respect to drugs, I am afraid there is still truth in his observation.

We are currently in a period wherein has appeared a number of new drugs and, as is always the case in such a situation, claims for them run the spectrum from hot to cold. Some reports would lead you to believe that the problems of human emotional distress and suffering can now be handled in the length of time it takes to write a prescription, while other investigators come up with pessimistic results, although these tend to be a little unpopular. As one tries to obtain perspective, and keeping in mind the rich historical experience with new drugs as they have appeared in decades past, it is more or less evident that we simply cannot say, as of 1955, what place these new agents may come to occupy in the years ahead. They are interesting and some appear to have a definite effect in allaying tension and anxiety. However, I would suggest that we adopt an attitude of watchful waiting about them and in reading reports on their use, insist within our own thinking that the results to which we give credence be based on research which has good controls built into the experimental design. Clinical research in drug treatment is admittedly a most difficult field because of the many variables other than straight pharmaceutical effects that always intrude into the picture. One important variable, to mention an example, is the enthusiasm, or lack of it, for the drug on the part of the physician giving it. This factor alone, and there are numerous others, calls for carefully controlled experimental design. For numerous reasons, adequate controls appear too seldom in work with the newer drugs.

*Presented at the Annual Meeting of the Manitoba Medical Association, October, 1955.

A word about the general philosophy of the use of drugs in psychiatric conditions may be in order. A drug may be a so-called "specific" and attack a disease reaction at its center, for example sulfa drugs and antibiotics in bacterial disease, or it may replace some deficiency of the body, such as insulin, thyroid extract, etc. Other drugs may alleviate symptoms but do not pretend to be specific and we have a host of agents in this category. Codein relieves a cough but does not cure pertussis, barbiturates relieve insomnia but do not cure a difficult marriage, amphetamine wakes a person up but does not cure lack of sleep, and so on in almost endless parade.

There is no drug known that is curative of any mental or emotional disorder, unless the cause of the mental disorder is due to a primary disease reaction which can be treated more or less specifically. A patient with central nervous system syphilis who is also grandiose and excited may be treated with penicillin, and, if caught before major hurt has been done to the brain, the penicilin therapy may see the mental symptoms disappear. However, in the vast majority of psychiatric cases, drug treatment is symptomatic. The drugs may alleviate symptoms, but they do not attack the basic psychologic disorder. A good illustration is found in a group of drugs we have used for years, the barbiturates. Any of the barbiturates often will relieve neurotic anxiety and make life a great deal more comfortable for the patient. However, when the barbiturates are stopped, the neurotic anxiety tends to reassert itself. In other words, the drug has relieved symptoms while it is being given, but it has done nothing to the basic pathology producing the symptoms. This is not to underestimate in any degree the great value of symptom-relieving drugs —after all they make up most of the drugs we use daily in our practices—but I point this out with some care because a few reports about the new drugs, particularly in the lay press, might lead one to believe that they cure mental and emotional disorder. There is no convincing evidence that these newer drugs do this. There is early evidence that several of them, however, may be better or less toxic symptom-relievers than we have had hitherto.

The newer drugs to which we might address ourselves today are:

I. Drugs which aim at reduction of tension or agitation.

1. Chlorpromazine ("Thorazine" SKF in U.S.A.;

"Largactil" SKF in Canada)
2. Rauwolfia derivatives
3. Miltown (Wallace), Equanil (Wyeth) (2 methyl2N propyl-1, 3 propanediol dicarbamate)

II. Drugs which aim at mood stimulation.
1. Meratran (Merrell) (alpha 2-piperidyl benzydrol hydrochloride)
2. Frenquel (Merrell) (gamma isomer of Meratran)

As used in emotional disturbance or psychosomatic disorder, they all have in common the hope of altering mood, either up or down. Either they aim at reducing tension or agitation or they aim at stimulating or elevating the mood in a depressed patient. Perhaps the best way of getting at them is to discuss each briefly and to make what comments one can as to their utility.

Chlorpromazine is derivative of phenothiazine. Developed in France, it has had extensive use in Europe. It was employed first as a preventive of nausea and vomiting and, as its sedative effects became better known, has been used extensively in psychiatric conditions, particularly those in which excitement, agitation, restlessness, tension, and overactivity are the terms used to describe the patients' conditions.

Chlorpromazine produces a number of physiological responses in the human, but the one I shall discuss briefly is the central depressant effect.

The drug can be given parenterally or orally, and the dosages used in various psychiatric conditions have shown a variation from 25 mg. per day to dosages of several thousand milligrams daily. In general, people working with the drug have tended toward the lower dosage range in nonhospitalized, ambulant patients and toward the higher doses in seriously disturbed, hospitalized, psychotic patients.

From the standpoint of the general physician or internist, I presume his major use of chlorpromazine in the pychiatric area of office practice might limit itself to persons who are tense or who have somatic symptoms based on tension. For example, at the University of Minnesota we have tried the drug in outpatients having anxiety reactions and psychosomatic disturbances. We have usually started at 50 mg. per day and have increased the dosage over a week or two to 200-400 mg. per day, depending upon the sedative action obtained. There is no question that the drug has a sedative and quieting effect, although, as I will mention in a moment, there is question as to whether it is always the drug of choice in these conditions.

As to untoward reactions and side effects. As common side effects one sees some feeling of light headedness, often on postural changes such as getting out of bed or up out of a chair (and this type of symptom probably relates to a relative hypotension). Syncope is quite ususual, however. Dry mouth and some resultant difficulties in swallowing may occur, and I have seen several patients become nauseated while taking the medication. By and large, the side effects of this variety are more of a nuisance than anything else, although now and then you will have to stop the drug or materially reduce the dosage because of a persistent and annoying side effect.

Complications of chlorpromazine are mainly:
1. Skin rash
2. Jaundice
3. Parkinsonian syndrome
4. Agranulocytosis

The jaundice is known to be due to intrahepatic biliary obstruction and not due to parenchymal damage to the liver. Stopping the drug sees the jaundice disappear without sequellae. The skin rash is treated in the same manner as is the Parkinsonian syndrome, i.e., stopping the drug.

The blood dyscrasia of agranulocytosis is by all odds the gravest of the complications; and while only occasional reports are yet seen in the literature, there is no doubt that it can occur. We have had two patients develop agranulocytosis, and without heroic treatment by the Department of Medicine, I am convinced, both would have had a fatal outcome. Fortunately, they survived. However, these two experiences have caused us to take a more serious attitude about the drug, not using it if there appears to be some less toxic agent that may help sedate the patient about as well. Patients who are receiving chlorpromazine are now followed routinely by weekly urine tests for bilirubin by the ictotest method for at least the first two months of treatment. During the same period an occasional white blood count should be done; and if the patient is unable to communicate well, the routine white blood count should be on a weekly basis. The patient is instructed to stop the medication if he develops a sore throat and to report this symptom to the physician.

I do not wish at this point to convey the feeling that chlorpromazine should not be used because of the risk of a blood dyscrasia. I do wish to mention, however, that this can occur, and it remains for the next several years to reveal how frequent an occurrence this may turn out to be. If frequent, chlorpromazine undoubtedly will have the history of Pyramidon which had to be discarded on this account. If very infrequent, chlorpromazine will become a valuable adjunct in the treatment of psychiatric disorders, both of major and minor varieties. In general, then, the indication for chlorpromazine is psychomotor overactivity, and the drug aims at reducing this.

As used by the general physician for psychiatric purposes, it would be my suggestion that if the patient is tense, distraught, restless, or has pychosomatic phenomena based on tension, the

first decision is whether or not the patient requires some relief via drugs. If you decide medication is indicated and if you foresee the need for using something over a fairly long period of time and during the day as well as night, chlorpromazine might well be considered. In the outpatient, one might start with 25 mg. orally two or three times daily and at bedtime. If this is not sufficient, go to 50 mg. three times daily. More often than not this will suffice in the ordinary situation. You can, of course, carry the dosage to considerably higher levels but usually this will do.

For this type of longer term use, chlorpromazine is, I believe, preferable to barbiturates and does not tend to cause the feelings of grogginess and "hangover" that are seen so often with barbiturates.

One other psychiatric use of chlorpromazine is in alcoholism. In acute intoxication, 50 mg. (intramuscularly if need be) usually produces sleep, but the patient can be easily aroused for the taking of fluids, etc. For this condition, I believe the drug is as good or better than any other agent. In delirium tremens the drug is also useful in controlling excitement and agitation.

Rauwolfia and its extracts. There is no cause for me to develop the history of rauwolfia serpentina and its extracts with a group such as this. Originally used in the treatment of hypertension, its sedative or tranquilizing effects were noted, and it was then tried in the mental and emotional disturbances. In general you can consider the indications for its use in the psychiatric area to be the same as those described for chlorpromazine. Indeed, the two are often used together and seem to potentiate each other, i.e., lower dosages of each can be employed than when used separately.

When used as the single agent to reduce emotional tension and distress, reserpine in the outpatient is usually started at 0.1 mg. orally two or three times daily and the dose increased from there. The dosage range is wide and the margin of safety apparently is tremendous. The highest dosage I have used is 32 mg. per day in an anxious patient (a physician, incidentally). I have used reserpine in about 50 outpatients and must confess I have mixed feelings about its value. I have not found it to produce consistent results in the tension states. The reports in the literature also show a good deal of variation in results obtained, and much more research is needed before we have valid information about its psychiatric value.

Side effects are fairly common but do not amount to much. Many patients will report nasal stuffiness and itching of the eyes, and in two of my patients this was so annoying they stopped the drug. Almost all outpatients report bizarre dreaming which they regard as rather interesting, since it is out of character from their usual dreaming. Some light headedness on change of posture (probably a hypotensive effect) is quite common. Infrequent side actions of Parkinson syndrome and ankle edema are also reported. (The physician I mentioned showed both of these phenomena in mild form.)

For the general physician, I believe that reserpine is worth a clinical trial in patients with mild tension states; and it produces very little, often no, feeling of drowsiness or "grogginess." I would suggest trying it for at least two or three weeks before forming a final judgment about it in an individual patient. If it works, it can be continued more or less indefinitely.

Again drawing from personal experience, I would suggest that you not use the drug in a patient who has any degree of depressed feelings. It seems to accentuate the depth of depression, and such patients may be more distressed on the drug than when they started it.

This is too brief a discussion of reserpine in psychiatry, but much of what I have said about chlorpromazine applies here as well. Both aim at the reduction of tension and hyperactivity. The position of reserpine in this respect still seems to be undetermined for the most part.

Miltown and Equanil. These are two of the newest of the so-called tranquilizing drugs to appear on the market. Chemically they are not related to the other sedative drugs. They were first synthesized in 1950 and in 1954 were reported as interneuronal blocking agents and muscle relaxants. Early animal and clinical studies indicated a mild sedative effect with little drowsiness and almost no toxic effects.

They are given in dosages from one to five or six tablets (400 mg. each) daily and like chlorpromazine aim at reducing tension and anxiety. There are too few reports in the literature as yet to even begin a critical evaluation of its merits. I can only say about it that it can be tried in these conditions. It appears to have the advantage that, at least, it does no harm. I have not yet seen any reports that describe toxic manifestations.

The agents so far discussed are used mainly for their sedative effects. There are two other chemically related compounds, Meratran and Frenquel, which are used primarily for their stimulant effects on the central nervous system. Hence these two agents, like amphetamine, find their chief indications in patients who complain of mild depression, inertia, loss of interest, and fatigue.

Meratran, used in daily doses from 2 to 25 mg. daily, has not shown dangerous toxic symptoms and is certainly worthy of trial in the patients

you see who have mild depression. Whether it is a better drug for this purpose than the older amphetamine is still undetermined. In the few cases in which I have used it, I cannot see that it does anything better than amphetamine, but again this is guesswork until controlled experimentation is done. It is reported that Meratran does not elevate blood pressure or increase pulse rate, and if these findings are borne out, it would be a safer drug than amphetamine in patients with cardiovascular disease. It deserves investigation in the treatment of narcolepsy to see if it is more effective than amphetamine.

Frenquel is used in daily doses of 10 to 50 mg. and for the same purposes as Meratran. I have personally never used this drug and since there are few reports in the literature, I cannot say much more about it. It has been found to have the interesting ability, along with a number of other agents, to block or prevent the experimental development of delirious or psychotic reactions in human volunteers upon giving mescaline or LSD-25. What this may mean in the field of psychiatric therapy is not known as yet.

In closing, may I mention again that these drugs have yet to find their true places in medical practice. Whether ten years hence they will even be remembered is a matter of conjecture. Several of them have been called "miracle drugs" in the lay press, but I would suggest that a critical and objective attitude is needed at this time until further research and clinical trial have had time to bring them into focus. None of them cure mental illness or neurotic reactions, but they are symptom relievers. Whether they will turn out to be better or less toxic symptom relievers than the ones we are well acquainted with, we must wait and see.

Before sitting down, I would like to express my gratitude for the honor you have done me in inviting me to your meeting. I appreciate it very much.

Medicine

Diagnosis and Treatment of Hyperthyroidism

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In the past ten to fifteen years, tremendous strides have been made towards an understanding of thyroid physiology, and subsequent upon them newer methods of diagnosis and treatment have arisen. It is often difficult for the physician to ferret out the most useful of the many newer diagnostic procedures from the multitude of techniques which are described in the literature. Similarly, it is difficult to take a firm stand on the proper method of treatment of hyperthyroidism. The methods of diagnosis and treatment selected are in the last analysis often dependent upon the facilities available and the particular type of patient concerned. It is interesting that the etiology and physiopathology of hyperthyroidism still remains obscure and, until the disease can either be prevented or attacked specifically, continued flux in the popularity of a given therapeutic regimen will undoubtedly continue to occur.

Diagnosis

The diagnosis of a well established case of hyperthyroidism, whether it be classical Grave's disease or a nodular toxic goiter, is a relatively easy problem. When the diagnosis of hyperthyroidism is obscure but suspected, every technique known to the physician is called upon. This is particularly true in the elderly group of patients with congestive heart failure and thyrotoxicosis—the so-called thyrocardiacs or patients with "masked hyperthyroidism". In the latter group recognition and treatment of the thyroid dysfunction may lead to a dramatic reversal of the cardiac failure.

In this era of complex and often very useful laboratory procedures it seems almost heresy to mention the importance of a good history and an exhaustive physical examination. The symptoms and signs of hyperthyroidism are known to every student. A simple listing of the evidence for and against the diagnosis is often very useful in arriving at a decision.

Determination of the Basal Metabolic Rate (B.M.R.), if properly carried out, still remains an excellent procedure which is available to almost all physicians today. Improper preparation of patients, faulty apparatus and the acceptance of curves which are obviously inaccurate have tended to detract from the value of the B.M.R. In clinics where meticulous B.M.R. determinations are made the correlation with the clinical state of the patient is about 80 per cent. An increase in metabolic rate unrelated to thyroid overactivity may be seen in hypertension, cardiac failure, pulmonary insufficiency, leukemia and the lymphomas. In those individuals where great difficulty is encountered in obtaining a satisfactory B.M.R. because of anxiety, the use of barbiturates prior to the determination is most useful. This so-called "somnolent B.M.R." tends to exclude some of the effects of tension since the basal value falls considerably while in hyperthryoidism only to a limited extent.

Delivered to the forty-eighth Annual Meeting of the Manitoba Medical Association, Winnipeg, Manitoba, October 26th, 1955.

The fasting serium cholesterol is probably the least useful of all the laboratory aids in the diagnosis of thyrotoxicosis. If found depressed, it is seized upon as a further bit of evidence in favor of a positive diagnosis. Certain anemias, infections, hepatic disease and chronic inanitition may produce a hypocholesterolemia and these must be taken into consideration in the evaluation of a low cholesterol. Although single cholesterol determinations are of little value, serial determinations as a guide to the efficacy of treatment is extremely useful.

Protein Bound Iodine (P.B.I.)

Iodine exists in the plasma as an organically bound or hormonal iodine and as inorganic iodine. Hormonal iodine is loosely bound to the albumin fraction of the serum proteins. Thus precipitation of the serum proteins separates these two forms of iodine and enables the laboratory to determine the hormonal iodine (P.B.I.). Normal values lie between 4 and 8 mg. per 100 cc. The determination involves extremely accurate and time consuming techniques and is not suitable for most routine clinical laboratories. Falsely high values are seen after the ingestion of organically bound iodine in the form of iodized oil, tetraiodophenolphthalein, priodax, etc., and may persist for as long as 3 years. Large amounts of inorganic iodine ingestion may lead to their binding with the serum protein and again give falsely high values.

The use of radioactive isotopes of iodine as an aid in the diagnosis of thyroid dysfunction was introduced fifteen years ago ([1,2]) and since that time many observers have demonstrated a significant correlation between the level of thyroid activity and the uptake of radioiodine. Measurement of the gamma rays which penetrate the tissue surrounding the thyroid, as the isotope disintegrates by sensitive counting techniques, is a very useful laboratory procedure.

Many methods of I^{131} tracer studies have been evolved in an attempt to achieve maximum accuracy, but as yet no procedure of appraising thyroid function is 100 per cent accurate. A positive correlation of the 24 hour I^{131} uptake with the final diagnosis is found in about 85 per cent of cases([3]). There is an inescapable overlap between hyper, hypo and euthyroidism. False values are obtained after the ingestion of inorganic iodine as exists in many cough medicines and this may inhibit uptake for up to 12 weeks. Organic iodine containing dyes so widely used in radiology today for gallbladder visualization, pyelography, myelography, bronchography, etc., may influence I^{131} uptake for 6 months or more. Antithyroid drugs, ACTH and the adrenal steroids all interfere with the accuracy of the procedure.

Radioactive iodine is absorbed into the blood stream as iodide and then selectively trapped by the thyroid or excreted in the urine. The distribution of I^{131} in the urine, the blood and the thyroid provides indices of thyroid activity. The techniques used vary from clinic to clinic as regards the size of the tracer dose and the optimal time at which the I^{131} uptake over the thyroid gland or its excretion in the urine is measured. Radioactive iodine uptake has been measured from 1 to 6 hours, 12 hours, 24 and 48 hours according to the practise of the particular clinic. The most commonly used index of thyroid activity today is the 24 hour uptake. The measurement of the 24 to 48 hour urinary excretion is no longer carried out extensively because it is more cumbersome and accuracy of urine collections is hard to achieve. More elaborate techniques measuring the distribution rate of radioiodine in the tissues have been evolved to increase accuracy, but these are not suitable for a routine laboratory.

An attempt to develop methods providing an answer within a short period of time has been made. These brief techniques require additional measurements over the thigh, since a significant fraction of the radioiodine is still circulating in the blood and tissues and this must be subtracted from the uptake by the thyroid gland.

Studies on the conversion of administered radioactive iodine into hormonally labelled iodine have been very useful adjuncts in difficult diagnostic problems. This has been expressed as the "conversion ratio" which is the serum P.B.I.^{131} (24 hrs) x 100 — Total plasma I^{131} (24 hrs.). This requires large doses of I^{131}, usually 100 microcuries, and separates hyperthyroids and euthyroids with great accuracy but is of little use in the diagnosis of hypothyroidism([4]).

A miscellaneous group of procedures have been evolved through the years such as the creatine tolerance test. These methods are, at best, indirect and also nonspecific and will probably never achieve great usefulness as a routine.

In the occasional patient where the aforementioned procedures are all equivocal a physician must resort to a therapeutic trial with iodine or one of the antithyroid drugs. The presence or absence of clinical and laboratory evidence of improvement during such a procedure can be of inestimable aid in the "borderline" patient.

Treatment

The methods of treatment of hyperthryoidism available and in common use today include: 1, Iodine; 2, Surgery; 3, Antithryoid drugs, alone or combined with iodine; 4, Radioactive iodine (I^{131}); 5, Potassium perchlorate. The particular method to be followed is dictated by the type of goiter, the patient's age and clinical state, the treatment available and often the physician's familiarity with and preference for a particular approach.

Iodine historically is the oldest method of treatment of hyperthyroidism, its favorable effects being described by Cheadle in 1869([5]). Today,

although iodine is never the preferred agent for the definitive treatment of hyperthyroidism, it plays several important roles. Its use as a therapeutic trial in doubtful cases of hyperthyroidism has already been described. Iodine is used by many surgeons in the pre-operative preparation of patients with mild hperthyroidism. In moderate or severe cases it is almost invariably used seven to ten days before operation either alone or in combination with the particular antithyroid drug employed to control the hyperthyroidism. In patients with hyperthyroidism who receive a therapeutic dose of I^{131}, iodine may be used to control symptoms until beneficial effects of I^{131} become apparent. This is imperative in patients with associated congestive heart failure. Although thyroid crises have become rare, the use of intravenous iodine either alone or combined with cortisone or hydrocortisone is the preferred method of treatment. Iodine is usually administered as Lugol's solution or as enteric coated tablets of potassium iodide.

Surgery continues to hold a strong place in the treatment of hyperthyroidism despite the advances made in the medical management of this disease. This is, in part, due to the fact that surgery is almost completely safe in patients adequately prepared with antithyroid drugs and iodine. The mortality rate of experienced surgeons is a fraction of one per cent (0.7%). However, the overall mortality and morbidity rate associated with thyroidectomy is much higher. The major disadvantages include: (1) Hypothyroidism (10-15%); (2) Recurrence of hyperthyroidism (Grave's disease) in approximately 5 to 15 per cent. (There is an inverse relationship between these two; the more radical subtotal thyroidectomy leading to a higher incidence of hypothyroidism, but a lower incidence of recurrence and vice versa); (3) Hypoparathyroidism; (4) Recurrent laryngeal nerve injuries.

The time lost from work, the expense of hospitalization and the discomfort associated with the operative procedure are of lesser import, although these are factors which should be taken into consideration.

Surgery is clearly indicated in a solitary nodular toxic goiter. The clinical behaviour of these patients suggests it is a separate entity from the hyperthyroidism of Grave's disease, perhaps due to a different type of hormone production by the solitary nodule. Hyperthyroidism occurring in large nodular goiters, particularly if pressure symptoms are a feature, is best treated surgically.

Although surgery is considered the preferred treatment for Grave's disease in some medical centres, it is our feeling that it should be reserved for those patients in which control by medical means is impossible to achieve. This is particularly true of young patients with Grave's disease in whom a very thorough trial of antithyroid drug therapy has failed and in whom the use of I^{131} is contraindicated because of age.

The antithyroid drugs first introduced by Astwood[6] in 1943 play a significant role in the modern management of hyperthyroidism. These substances block the enzyme activity concerned with the oxidation of iodide to iodine and thus prevent the formation of the thyroid hormone. Hyperthyroidism can regularly be controlled by the administration of these agents, and a euthyroid or hypothyroid state can be maintained for as long as treatment is continued.

Table I

Antithyroid Drugs Available

(1) Methylthiouracil.
(2) Propylthiouracil.
(3) Iodothiouracil.
(4) Tapazole - Methimazole
(1 Methyl, 2 Mercaptoimidazole)
(5) Neo - Mercazole
(2 - Carbethoxythio - 1 - Methyl Glyoxaline).

The antithyroid drugs available are listed in Table 1. The initial effective dose of propylthiouracil or methythiouracil is approximately 200 to 600 mg. per day, whereas with tapazole or neomercazole 20 to 70 mg. per day is necessary. When a euthyroid state is achieved the minimal effective dose is arrived at.

The antithyroid drugs are indicated in the following circumstances: (1) The pre-operative preparation of patients with hyperthyroidism combined with iodine for 7 to 10 days before the surgical procedure, the latter producing a decrease in vascularity of the gland. It is not at all certain whether the combined use of iodine and an antithyroid drug produces a more rapid remission than the antithyroid drug alone. (2) The long-term treatment of Grave's disease in the hope of producing a lasting remission. (3) The treatment of hyperthyroidism during pregnancy, a circumstance in which these agents have proved highly effective. (4) The control of severe hyperthyroidism in the period between I^{131} administration and the appearance of a beneficial effect. The antithyroid drugs are a highly effective form of therapy for hyperthyroidism in areas where no I^{131} is available and in patients in which surgery is considered unsafe.

The disadvantages inherent in the use of the antithyroid drugs are 1, The toxic side effects; 2, The higher incidence of post treatment recurrence; 3, The necessity of cooperation of the patient in the medical management program; 4, The lower incidence of permanent remission in nodular goiter or in post-operative recurrence of Grave's disease.

New antithyroid drugs have been developed in the hope of increasing their effectiveness and

decreasing toxicity. We still prefer propylthiouracil and use it extensively. The incidence of untoward side effects is 1 to 2 per cent, and these are usually minor skin rashes or fever. More rarely a severe dematitis arises and very rarely agranulocytosis. Patients should be instructed in the possible significance of a sore throat, skin rash or fever. Occasionally hypothyroidism with associated enlargement of the thyroid gland is a feature. This assumes particular importance in malignant exophthalmos and it is sometimes difficult to arrive at a maintenance dose of an antithyroid drug. The concurrent use of thyroid permits an adequate "blocking" effect without initiating hypothyroidism and thus encouraging pituitary hyperfunction.

Treatment with an antithyroid drug is usually continued for one year after euthyroidism has been achieved. There is a considerable divergence of opinion on the incidence of prolonged remission after cessation of therapy. In a study of 101 hyperthyroid patients observed for four years after the conclusion of a course of antithyroid drug therapy, 55.5 per cent remained euthyroid.[7] Several courses of treatment increased the remission rate to 70.3 per cent. The frequency of recurrences decreased gradually as the duration of remission increased. A decrease in goitre size during treatment was found to significantly improve the ultimate result. It has been shown that primary hyperthyroidism in a young individual with a small diffuse goitre also favors the occurrence of a prolonged remission. One advantage to medical management with an antithyroid drug is the intactness of the thyroid gland when a permanent remission is produced.

The importance of antithyroid drugs and of surgery in the treatment of hyperthyroidism has been somewhat overshadowed by the therapeutic use of radioactive iodine. (I^{131}) Its use in the hyperthyroidism of the Grave's disease type is widely accepted as the most efficient therapeutic method. McCullagh and his associates[8] at the Cleveland Clinic have had extensive experience with its use and report only two failures in 1,235 patients with Grave's disease. They have noted only 8 relapses of hyperthyroidism in this series of which only two could be classified as true recurrences, the remaining six having persistent hyperthyroidism.

Radioactive iodine therapy is most clearly indicated in cases of: (1) Grave's disease in patients over 40 years of age. This age limit was at first introduced because of the possibility of producing cancer many years after treatment. In the thousands of patients so treated this has not been borne out, and the age of the patient is gradually becoming decreasingly important, if other indications are present. The possibility of a carcinoma arising in an I^{131} treated gland unrelated to the therapy must be entertained since such diffuse glands occasionally harbor small carcinomas; (2) Recurrent hyperthyroidism after surgery or adequate antithyroid drug therapy; (3) Severe cardiac disease; (4) Old age and other concurrent disease; (5) Preference of either the physician or the patient.

The advantage of I^{131} therapy in Grave's disease are: (1) The absence of mortality to date. (2) The absence of permanent tetany and cord paralysis. (3) The high apparently permanent remission rate. If recurrence occurs it can be easily treated with additional I^{131}. (4) There is no discomfort, no serious disability and minimal time lost from work.

The major disadvantage of radioiodine therapy is the development of hypothryoidism. The incidence varies rather widely (4 to 20 per cent) being in part dependent upon the particular centers desire to produce a remission with one dose of I^{131}. In these, hypothyroidism is more prevalent than in centers where a more cautious approach to dosage is used. McCullagh et al[8] have reported a 9 per cent incidence of permanent hypothyroidism in a survey of 325 cases.

In individuals with severe congestive heart failure, the three to eight week interval between I^{131} administration and the development of a therapeutic effect is a theoretical disadvantage. This can be in part overcome by the administration of either iodine or an antithyroid drug. Rare instances of exacerbation of hyperthyroidism intensifying cardiac failure and precipitating a thyroid storm because of thyroid gland breakdown following treatment has been reported.[9]

I^{131} therapy is contraindicated in pregnancy but does no harm during the first 14 weeks of gestation since the fetal thyroid has an insignificant I^{131} uptake until that time.[10] It might be argued that I^{131} therapy alters the thyroid gland and does not treat the disease at its source, but these factors are of little practical importance.

The estimation of I^{131} dosage remains one of the most difficult problems to solve in this field. Dosage is determined in most medical centers on the basis of one or more of the following criteria: (1) Size of the thyroid gland. This is a very difficult measurement to estimate with any accuracy. (2) Twenty-four hour I^{131} uptake. (3) Biological half life. (4) Age of the patient. (5) Urgency of cure. (6) "Clinical judgment".

Two to three months after the initial dose, the patient is evaluated clinically and by whatever laboratory procedures are deemed necessary. If only partial control of hyperthroidism is found and the patient no longer continues to improve, a second dose is administered. In most clinics approximately 75 per cent of patients are controlled with a single dose.

The estimation of dosage in nodular toxic goiters is fraught with even more difficulty. No good criteria are available and in many clinics a

large dose ranging from 30 to 50 millicuries is administered. This type of therapy for nodular toxic goiter should be reserved for those cases in which surgery cannot be accomplished safely.

The latest form of therapy in Grave's disease concerns the antithyroid effect of potassium perchlorate. Morgans and Trotter[11] have reported good control in a series of patients treated with this agent, although it is achieved more slowly than with the usual antithyroid drugs. It is of no use in the preparation of patients for thyroid surgery. No toxic effects were noted in 108 hyperthyroid patients so treated.

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Diagnosis in Arthritis

S. D. Rusen, M.D.

The classical pictures of rheumatoid arthritis and osteo arthritis are well known and usually easy to recognize. Acute arthritis, and the early chronic cases, may be difficult problems in differential diagnosis. Yet, it is of more than academic importance to identify each particular case. Conditions of widely differing etiology have a common denominator of pathology, i.e. of one or several inflamed joints. To label a case as "arthritis" without pursuing a more specific diagnosis is equivalent to diagnosing asthma, or epilepsy, without further clarification. The various types of arthritis have always implied great differences in prognosis. In recent years these differences have also had important bearing on treatment. The proper use of such agents as Benemid, colchicine, steroids ACTH, and X-ray therapy depend on a precise diagnosis of the type of arthritis.

Before attempting to classify the condition one must be sure that arthritis is indeed present. Pain in a joint does not mean arthritis any more than pain in any location means organic disease. A definite diagnosis of arthritis should be based only on objective evidence, which includes swelling, effusion, heat, limitation of movement, and significant radiological findings. Often pain in fibrous tissue or muscle near a joint is erroneously accepted as being due to joint disease. This has even led to the absurd diagnosis of "periarticular arthritis." Pain in a joint may also be referred, as in the well known shoulder pain of coronary disease.

It should be more widely recognized that joint pains may be a manifestation of psychoneurosis. This, so called psychogenic rheumatism is not infrequently encountered. Sometimes the patient is a young person whose persistent joint pains have called forth a diagnosis of rheumatic fever, but who never develops any objective joint signs or heart lesions. Or the patient is middle aged, with insignificant degenerative changes, and diagnosed as osteoarthritis. The problem may be complicated too by compensation and pension factors.

A simple classification is the one adopted by the American Rheumatism Association.

Classification

1. Arthritis due to Specific Infection, e.g. Tuberculosis.
2. Rheumatic fever.
3. Rheumatoid Arthritis.
4. Osteoarthritis.
5. Traumatic Arthritis.
6. Gout.
7. Spondylitis.
8. Neurogenic Arthropathy, e.g. Charcot's Joint.
9. Diseases with which Arthritis is frequently associated, e.g. Other Collagen Diseases.

Rheumatoid Arthritis

The common form of onset is as a symmetrical peripheral polyarthritis. The difficulty of recognition is increased when it presents as an acute polyarthritis resembling rheumatic fever, or as a mono-articular disease. In such cases the diagnosis cannot be definitely established until the passage of time and subsequent events settle it.

Any one of the collagen group—disseminated lupus erythematosus, periarteritis, scleroderma, dermatomyositis may exhibit a peripheral arthritis indistinguishable from rheumatoid.

Reactions to drugs and other allergic phenomena may enter into the differential diagnosis. Polyarthritis subsequent to penicillin therapy is not rare. Peripheral arthritis may be the presenting complaint occasionally in bronchogenic carcinoma. Anyone treating a case of foot strain or flat feet or metatarsalgia should keep in mind the possibility of early rheumatoid arthritis.

Examination of the hands is generally the most rewarding and the most convenient procedure. Here are several dozen diarthrodial joints quite close to the surface. Minor degrees of limitation of

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movement are more easily noticed. Joint tenderness is easily elicited. A diminution in strength of grasp may be significant. The most common cause of wasting of the small muscles of the hand is rheumatoid arthritis. X-ray of the hands and wrists also are the most rewarding of any part and will often show detail not possible for deeper structures.

Anemia and rapid sedimentation rate are usual findings. One should avoid the diagnosis in the presence of a normal sedimentation rate. Where the anemia is marked, this arouses particular search for blood components, and splenomegaly, with the possible indication for splenectomy.

Other aids in the diagnosis, of occasional value, are:

1. Biopsy of synovial membrane.
2. Biopsy of a subcutaneous nodule.
3. Serological tests, e.g. sensitized sheep red cell agglutination[1].

Osteoarthritis

Degenerative changes of the joints are present in almost everyone past the age of 40. Because of their ubiquitous occurrence—x-ray findings alone are insufficient grounds for diagnosis. Similarly, grating of joints on movement is of no importance. When degenerative joint disease is responsible for symptoms, usually there is limitation of movement and X-ray changes in advance of the expected degree for that age. Osteoarthritis is usually easily differentiated from rheumatoid, although both being common conditions, they may occur simultaneously. Generally, in degenerative joint disease there is no effusion, or heat, anemia or rapid sedimentation rate. An exception is occasionally seen in the knee joints where osteoarthritis sometimes evokes mild and transient effusion and increased heat.

In the fingers osteoarthritis involves the terminal joints. In a small percent of cases the proximal interphalangeal joints may also be involved and this may cause confusion with rheumatoid[2]. In these cases there is absence of weakness and muscle wasting and X-ray findings are helpful.

Brain and others have emphasized the role of cervical osteoarthritis as a cause of compression of the spinal cord and nerve roots with production of a neurological disturbance which is baffling unless this condition is kept in mind.[3, 4]

The presence of marked changes in the spine may also obscure the diagnosis of a more significant finding such as bone tumor or multiple myeloma.

Rheumatoid Spondylitis

Any persistent or recurring backache, especially in a young man, warrants X-ray study of the sacro-iliac joints. Early changes may be noted here in a case with only mild limitation of movement. Systemically the changes encountered in rheumatoid arthritis are also present here.

It is well to remember that a patient with severe limitation of lumbar movement may still be able to touch his toes by means of hip flexion.

Diminished movement of the chest wall and a lessened resistance to pulmonary infection is a lesser known feature of spondylitis. Diffuse or girdle types of chest pain may occur. In 10% to 20% of cases peripheral joints may be involved.

It is of interest to note that identical sacro-iliac changes may also occur in Reiters syndrome.

Gout

The incidence and severity of this ancient and respectable illness is diminishing, but still occurs often enough to trap the unwary. It not rarely occurs within a few days after a surgical operation and still not rarely is diagnosed as cellulitis or thrombo phlebitis. Elevation of the blood or serum uric acid is helpful in confirmation of the diagnosis, but not essential.

When the acute attack is in a location other than the big toe, the diagnosis is easily missed. Acute gout may also involve two or three locations at once.

Chronic tophaceous gout is an uncommon disease in Manitoba. An advanced case may present severe and multiple joint deformities easily mistaken for rheumatoid. The demonstration of uric acid crystals in the tophus is a simple procedure and is pathognomonic.

Arthritis Associated with Genito-Urinary Disease

In this group are included cases with various combinations of urethritis or other lower genito-urinary infections, with arthritis, and ocular manifestations. The urethritis may be gonococcal, or more frequently non specific. The arthritis is in one or several joints, especially in the lower limbs. Repeated attacks are the usual history, and residual joint damage may occur. The textbook picture of gonorrheal purulent and destructive arthritis is rare. Keratodermia and other skin lesions may occur.

The etiology of this well known syndrome is unknown. Bacteriological evidence of gonococci is lacking in the majority of cases. Virus, spirochete, and pleuro pneumonia organisms have been incriminated, as has sensitivity to gonococcus or other organisms. An imposing array of antibiotics has been tried and found ineffective.

Summary

It is apparent that the differential diagnosis of arthritis is made more difficult by the circumstance that joints can only react to disease in one way, whatever the disturbing factor. It is mostly by their accompaniments that we distinguish them. Much recent research is devoted to diagnosis by means of changes in blood serology and in the synovial fluid. While not yet in wide use, this promises to be a fruitful field for investigation.

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Lead Poisoning in an Adult Caused by Therapeutic Doses of Lead Acetate

Murray Campbell, M.D.

Lead poisoning due to therapy is extremely rare in adults. A search of the available literature of recent years including the monograph by Cantarow and Trumper[1] disclosed only one report of two such cases by Christophers in the Australian Medical Journal[2]. In both cases the drug was administered by Chinese herbalists.

The following case is worth reporting because of its rarity.

Case Report

A fifty-year old white woman was admitted to the Winnipeg General Hospital on September 7th, 1955 for the treatment of post-menopausal bleeding, likely estrogen-induced. Other symptoms were intermittent diarrhoea for six months, weakness, a loss of eighteen pounds during the past year and "stumbling" for a week or ten days. The gynecological complaint was investigated and treated. A routine blood count showed 3.3 million RBC's with a hemoglobin of 8.5 gms (55%) and a colour index of .83; cell volume 28%, MCV 86, MCH 25.6 and MCHC 30.5. It was felt that the uterine bleeding was insufficient to account for the degree of anemia, and the patient was referred to Medicine for further investigation. A bone marrow aspiration was done, and it was found to contain red blood cells with basophilic stippling. The blood smear was rechecked and here too stippling was found. A short (2 cm.) but typical lead line was found on the gingival margin of the lower gum, the upper jaw being edentulous. The urine was examined for coproporphyrins and found to be positive, both spectroscopically and with ultra-violet light.

An enquiry to the referring physician in the town where the patient lived elicited the fact that she had received lead and opium pills from August 1st to August 10th, and again from August 19th to August 29th for her diarrhoea. The total amount received was one hundred and twenty grains of lead acetate. The "stumbling" consisted of difficulty in lifting the feet when going upstairs, suggesting early foot-drop. There were no neurological abnormalities demonstrated on September 14th, but by that time the stumbling was considerably improved. There was no suggestion of peripheral neuritis in the upper limbs, and no other manifestations of lead poisoning.

As has been noted in this case that the lead line was present only on the lower gum, and this is in agreement with Aub[3] who states that it is almost universally absent where the teeth have been removed. There seems to be little doubt that poor dental hygiene and gingivitis increase the rate of development and intensity of the lead line. It can however occur in healthy gums. In this patient the teeth were dirty and pyorrhoea was evident. The lead line was very faint, but still noticeable three months after exposure. It usually persists for several months according to Aub[3].

Because of the relatively short length of exposure and the early spontaneous improvement in the "stumbling" and hemoglobin which rose from 55% on September 7th to 62% on September 16th, it was decided not to use a chelating agent, but to attempt to speed improvement by giving two quarts of milk daily. Because of weight gain this was changed to skim milk at the patient's request. Subsequent events justified this course. On October 1st, the hemoglobin was 72% and on December 1st, 84%. On the latter date the patient had no symptoms and the diarrhoea had not recurred. The latter had been thoroughly investigated in hospital, and no cause ascertained.

In summary, a proven case of lead poisoning due to the administration of lead acetate in therapeutic doses over a short period has been presented, and the sparsity of such reports in present day literature noted.

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Gynecology

Culdoscopy

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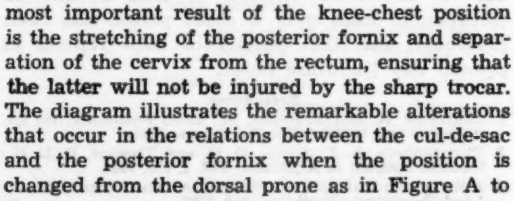
Endoscopic examination of the abdominal viscera has been performed with variable success for almost half a century. A great advance in this method of investigation was the introduction of gas into the abdominal cavity, thereby lifting the anterior abdominal wall from the bowels and preventing their injury during insertion of the trocar and cannula. The endoscope in use in 1919 was especially adapted for examination of the pelvic viscera and became known as the peritoneoscope. Improvements in peritoneoscopy were constantly reported, but, due to the presence of adhesions and loops of bowel, there remained dissatisfaction with the number of times an adequate view of the pelvic viscera was obtainable. This led to attempts to perform the examination through the posterior vaginal fornix with the patient in lithotomy position. Due to leakage around the cannula it was difficult to achieve and maintain adequate pneumoperitoneum, and in any event the bowel completely obscured the view. Then Decker conceived the brilliant idea of doing the examination with the patient in the knee-chest position. This position creates a negative pressure so that air rushes into the peritoneal cavity as soon as the trocar is removed from the cannula. This produces in effect a pneumoperitoneum and permits the bowel to fall forwards towards the diaphragm thereby leaving the pelvic viscera completely exposed to inspection. An additional and most important result of the knee-chest position is the stretching of the posterior fornix and separation of the cervix from the rectum, ensuring that the latter will not be injured by the sharp trocar. The diagram illustrates the remarkable alterations that occur in the relations between the cul-de-sac and the posterior fornix when the position is changed from the dorsal prone as in Figure A to the knee-chest as in Figure B. In the lithotomy



from Decker

position the cul-de-sac and the posterior vaginal fornix are narrow cavities almost parallel to each other and separated only by retroperitoneal tissue. In the knee-chest position both cavities become stretched with the peritoneum, forming the anterior wall of the cul-de-sac, draped over the domed posterior vaginal fornix. By 1946 Decker and others had developed culdoscopy to the point where it became a routine procedure.

It is not my intention to describe the procedure in detail; this has been done by Decker. A brief summary of the procedure seems necessary in order to appreciate at once the scope and limitations of culdoscopy. When we first started using culdoscopy we experienced considerable difficulty in maintaining the patient in the proper position, particularly when she was under general anaesthesia. It was not until we abandoned all sorts of slings and other devices designed to give support that we realized how easily a single assistant can balance the patient, provided the shoulders are properly braced and the thighs perpendicular to the top of the table.

One of the advantages of culdoscopy is that it can usually be done under local anaesthesia. However, the great majority of our culdoscopies have so far been done under general anaesthesia because it seemed that in this way more time could be taken with the examination, and the findings could be demonstrated to internes and others interested in learning the technique. The patient should not be placed in the knee-chest position without first performing intubation. If local anaesthesia is to be used it is well to precede the examination with a generous dose of morphine or Demerol. Spinal and saddle block anaesthesia are also recommended, but we have no experience with either of these agents as yet.

As already stated, the knee-chest position stretches the posterior fornix. Ample exposure of this area can be obtained with a retractor placed against the posterior wall of the vagina, and the tip of the blade depressed posteriorly. Simultaneously, the cervix is drawn downwards and forwards with a tenaculum attached to the posterior lip. In most cases this produces a distinct dome which is the site for insertion of the trocar and cannula. In cases where this dome does not clearly develop, the general tendency is to insert the cannula too near to the cervix for fear of injuring the rectum. This is unnecessary for the absence of a dome is not an indication that the rectum is actually dangerously close. In such cases it is best simply to select a site that is midway between the cervix and the posterior vaginal wall. The cannula and trocar are poised in a direction parallel with the spine and driven through the posterior fornix with a quick thrust. Any hesitation at this point may cause the peritoneum to separate from the vaginal wall and

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prevent entry into the cul-de-sac. Having inserted the cannula, the valve near the outer end is opened or the trocar simply removed to permit entry of air into the peritoneal cavity. The hiss of air rushing in is a reassuring sound and means that the cannula is properly placed and the examination can begin.

Since the image seen through the telescope is not distorted, no skill has to be acquired in interpreting what is seen. In the beginning, however, there may be some difficulty getting oriented, but this can quickly be overcome with practice. In order to bring the adnexa into view it may be necessary to press on the anterior abdominal wall and to manipulate the telescope over a wide range. Moving the tenaculum back and forth also helps.

Generally speaking, the only contra-indications to culdoscopy are a uterus fixed in retroversion or some other mass in the cul-de-sac which cannot be dislodged. It is probably not wise to attempt the examination in young girls.

As there is no precise set of indications for culdoscopy, the range of usefulness of the instrument increases as the skill and confidence of the operator increase. However, culdoscopy is chiefly indicated in patients suspected of having an ectopic pregnancy. Until we have acquired a larger experience it will not be possible to assess its value in this regard completely, but there is no doubt that many patients will be saved needless days of observation in hospital, while others will be spared the certain hazards of delay. In balance it appears to be true that the number of unnecessary laparotomies will be reduced—an obvious and great advantage of culdoscopy.

At the time of this review only 26 culdoscopies had been done at the Winnipeg General Hospital. Such a small number of cases is, of course, insignificant but there is no need to prove its value here, since it has been done many times by Decker and others. However, the results of even this small series leave no doubt of its value in the management of difficult diagnostic problems. In 4 cases the primary clinical diagnosis was ectopic pregnancy, but culdoscopy ruled this out in all but one. There was one case, however, where the examiner could not be certain of the origin of the blood that was visible in the cul-de-sac. A colpotomy was done and this proved the source to be a ruptured corpus luteum. In one case the cause of the symptoms was clearly established as chronic salpingo-oophoritis; in another the pelvis was normal and the final diagnosis was functional uterine bleeding.

In 8 cases ectopic pregnancy was the secondary diagnosis. The primary diagnosis was tuberculous salpingitis in 1 of these patients; chronic pelvic inflammatory disease in 3; functional uterine bleeding in 1; threatened abortion in 2; complete abortion in 1. The patient thought to have tuberculous salpingitis was kept in hospital for 3 days, during which time she showed steady improvement; but since ectopic pregnancy could not be ruled out definitely, it was decided to do a culdoscopy, and this revealed an ectopic pregnancy of the left tube. One of the patients with pelvic inflammatory disease had a unilateral adnexal mass making it necessary to rule out positively an ectopic pregnancy. At culdoscopy all but the adnexa was clearly visualized. No blood was evident but it was felt that a laparotomy should be done. The mass proved to be a tubo-ovarian abscess. Threatened abortion occasionally mimics ectopic pregnancy rather closely. In one of the two cases of this type the pelvis proved to be completely normal on culdoscopy, but in the other the examiner could not satisfy himself that ectopic pregnancy had been ruled out because he failed to get a good view of one side. At laparotomy the pelvis agaln proved to be normal. In retrospect it seems likely that this laparotomy could have been avoided if the examiner had had more experience. In the remaining cases ectopic pregnancy was definitely ruled out.

A miscellaneous group of 11 cases illustrates the broad application of culdoscopy. One young woman developed a mass in the pelvis following excision of a fibrosarcoma some months previously. There was natural concern that this might be metastatic. Culdoscopic inspection revealed normal ovaries and numerous peritubal adhesions.

Endometriosis is often diagnosed on grounds of the history and pelvic findings, but only rarely so with conviction. Such patients are therefore not infrequently denied definitive treatment. One of the patients in this group complained of pelvic pain and irregular bleeding and was diagnosed as having functional uterine bleeding. At the time of diagnostic curettage an impression was gained by the operator that the patient might well have endometriosis. In order to establish a positive diagnosis the pelvis was examined with the culdoscope and the signs of endometriosis clearly visualized.

Frequently the conviction that pelvic pain is of psychosomatic origin turns to doubt as the patient continues to complain. In dealing with such cases one is often at a disadvantage until one can be certain that there is indeed no pathology in the pelvis. In the past this has occasionally led to the performance of a laparotomy as a final effort to convince both patient and surgeon that there is no local disease. On the other hand, the natural reluctance to operate on such cases may lead to needless suffering. In three cases the pain complained of was of this sort, all being under the care of a psychiatrist. One of them complained of a severe pain in the right lower quadrant precipitated by menstruation. Each time she reported

an elevated temperature but findings on pelvic examination were always normal. Nevertheless, in order to be sure that nothing was overlooked and rather than dismiss the complaint as being psychosomatic, the pelvis was examined with the culdoscope and proved to be normal.

Culdoscopy is also of great value in the more specialized fields such as investigation of infertility and certain endocrinopathies. Hysterosalpingography will divulge only tubal obstruction but not its exact nature; a diagnosis of tuberculous salpingitis will certainly have an important bearing on the management of such a case. Stein-Leventhal syndrome is rare and the diagnosis may be difficult to establish without examining the ovaries directly.

Unfortunately it is not always easy nor even possible to enter the cul-de-sac. In 3 of the 26 cases reviewed the attempt had to be abandoned. Once the failure was due to lifting of the peritoneum from the vaginal wall. In such an event Decker recommends immobilizing the vaginal wall with Allis clamps and making an incision through it with a knife. This procedure is probably best not attempted in the early stages of the use of this instrument.

In spite of the obvious advantages of culdoscopy, its adoption as a routine procedure has been slow and halting almost everywhere. The reasons for this are not easy to find. When vaginal hysterectomy first became popular a decade ago, almost everyone doing gynaecological surgery made it his first duty to become proficient in this operation. There has not been nearly the same zeal in becoming proficient in culdoscopy. This certainly cannot be attributed to the dangers and complications of culdoscopy; very few have been reported. In any case the complications are as nothing compared to those pursuant to laparotomy. Nor is it a difficult technique to learn. Any one familiar with the anatomy of the cul-de-sac can teach himself quite handily. Many undoubtedly feel that they can manage about as well without, as with a culdoscope but anyone who has developed any experience with this instrument is convinced of its usefulness.

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Surgery

Infantile Hypertrophic Pyloric Stenosis

A Review of 100 Consecutive Cases Treated by Surgery*

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One hundred cases of Infantile hypertrophic pyloric stenosis were treated by surgery at the Winnipeg Children's Hospital during the period from January 1st, 1944 to May 5th, 1955. Since this is a fairly large series of cases, and, since the results compare favourably with those reported by other workers[1-6], it was considered that a review of this series of cases would be of interest to physicians and surgeons concerned with the diagnosis and the surgical treatment of infants.

Clinical Features

As in other reported series, males were predominantly affected in an approximate ratio of five males to one female. At the time of admission to hospital the ages of the infants varied from ten days to twenty weeks with the majority being admitted between the fourth and sixth week of life.

The average duration of symptoms was two to three weeks, but varied from one day to eight weeks.

While a history of vomiting was obtained in all cases, in ninety-three the vomiting was severe and projectile in nature. Ninety-four infants had lost weight or had failed to gain. Almost all babies had been healthy and of normal weight at birth. While a few infants regurgitated feedings from birth preceding the onset of vomiting, the vast majority of babies had taken their feedings without difficulty up to the onset of symptoms. Vomiting was not associated with abdominal pain, and even immediately after vomiting, the babies were hungry and would eagerly take another bottle. In no case was there bile in the vomitus. The reason for this is obvious, as the pyloric obstruction is proximal to the ampulla of Vater, and the bile cannot regurgitate back into the stomach. A history of projectile acholic vomiting in an infant (particularly a male) between the ages of two and six weeks, accompanied by a loss of weight or failure to gain, should at once suggest the diagnosis of infantile pyloric stenosis.

The signs of hypertrophic pyloric stenosis are mainly those of dehydration, visible intestinal peristalsis, and a palpable pyloric tumor. Seventy per cent of the infants in this series were dehydrated. In fifty percent of cases the dehydration was mild. It was moderate in sixteen percent, and severe in five percent of cases. The derangement of body fluids and electrolytes can be very serious. The loss of hydrochloric acid and fluids produces dehydration and alkalosis. In severe

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instances, alkalotic tetany may occur or potassium depletion may become marked. Eight infants with moderate or severe dehydration had preoperative blood chemistries performed. In five of these, the results were indicative of alkalosis.

In ninety-one of the infants, waves of gastric peristalsis were seen. Typically, these progressed across the upper abdomen from left to right during or immediately after feeding. In eighty-four percent of cases, a firm pyloric tumor was felt in the right upper quadrant of the abdomen under the liver edge. Patience and gentleness are required for the successful palpation of a pyloric tumor. The abdomen is exposed, the knees are slightly flexed, and during palpation the infant should be given a bottle of sugar water so that the child will lie quietly with the abdominal wall relaxed. Palpation is best done with the tip of the middle finger. Sometimes it is necessary to examine the infant on several occasions, before one can definitely feel the mass. Occasionally a tumor will only be felt after the infant vomits or after gastric aspiration, as a full stomach may make palpation difficult.

In older reported series of cases of pyloric stenosis, it was usual to find that most of the infants were breast fed. This, however, is probably only a reflection of changing pediatric management, in that, in our series of one hundred cases, over seventy-five percent of the infants were artificially fed. The weight of the babies on admission to hospital varied from 2,300 to 5,016 grams with an average of 3,598.

In only one infant was another congenital lesion seen. This baby had congenital heart disease. If infantile pyloric stenosis is considered to be a congenital developmental, overgrowth of the circular muscle coat of the pylorus, then it is gratifying to note that the incidence of other associated anomalies in pyloric stenosis, as compared to other congenital defects, is rare.

X-Ray Findings

Barium meal examinations were performed in thirty-seven percent of cases for the purpose of confirming or making a diagnosis. Typical x-ray findings include a dilated stomach, a persistent narrowing of the pyloric canal (string sign), and prolonged gastric retention of barium. Since barium meal in this condition has a slight risk, as vomiting with aspiration of barium may produce a serious chemical pneumonia, this procedure should be reserved for cases in which the diagnosis is in doubt and when one cannot feel a definite pyloric tumor.

Treatment

1. Preoperative Care

If dehydration is marked, the restoration of body fluids and electrolytes is regarded as urgent, but the operation itself is not an emergency. Twelve to twenty-four hours of preoperative preparation is frequently necessary. In this series of cases, seventy-four infants were sufficiently dehydrated to require fluids either intravenously or by hypodermoclysis. The types of fluids administered were mostly glucose in water or saline. In several instances, parenteral solutions containing 1/6 molar lactate and potassium were used. Twenty-two of the infants showed anemia and received blood transfusions. If the infant will retain some oral feedings, small amounts of Dextrose and Saline (oz.—q.2.h.) by mouth will frequently be tolerated well, and will help to correct dehydration.

In every case, a small stomach tube was passed through the nostril and into the stomach one hour preoperatively, and the stomach was irrigated with normal saline and completely emptied. This procedure reduces gaseous distension thus rendering the operation easier, prevents vomiting and possible aspiration during anaesthetic induction, and rids the stomach of decomposing food and mucus. The tube is left in place during the operative procedure, but is removed after the child has recovered from the anaesthesia. A number ten urethral rubber catheter with extra holes cut at the tip was found to be superior to polyethylene tubing for gastric lavage.

Small doses of subcutaneous atropine (grs. 1/300) were administered routinely prior to anaesthesia.

2. Operative Procedure

Ether with oxygen, or ether, nitrous oxide, and oxygen were the most frequently employed anaesthetic agents. Endotracheal intubation is preferred by the anaesthetists in this hospital. With this method, anaesthesia is smooth, an adequate airway is assured at all times, and the risk of intratracheal aspiration of gastric contents during handling of the stomach is minimized.

The type of abdominal incision employed varied considerably depending upon the particular choice of the individual surgeons on the staff. In forty-three cases, a right rectus muscle splitting incision was used; in twenty-seven cases a right rectus retracting incision was utilized; while in five a right upper quadrant gridiron incision was employed. In twenty-four cases the surgeons did not describe the type of incision used and, thus, the surgical approach was not known.

In all instances a pyloric tumor was present at operation, and a Ramstedt pyloromyotomy was performed. The method of dividing the pyloric sphincter varied slightly. Initially all surgeons incised the serosa overlying the pylorus in the bloodless line along the anterior superior aspect of the tumor. Some then used the blunt end of a scalpel for complete division of the encircling muscle fibres, while others used the points of a

haemostat. One surgeon used the tip of the left thumb and middle finger for division of the last few fibres at the duodenal fornix. This manoeuvre may have the advantage of minimizing the danger of mucosal perforation at this critical site.

The only operative complication occurring during this series of one hundred cases was accidental perforation of the duodenal mucosa. This occurred in eight instances. In two cases, the accident was not recognized and these two infants continued vomiting for ten days postoperatively and required a further operation to close the leak. In the others, the perforation was recognized at the time, and the hole was adequately closed. Following division of the pyloric sphincter fibres, it is important to squeeze the stomach, forcing air through the pyloric canal so as to make any mucosal leak obvious.

The suture material used for wound closure also varied considerably. Over half of the surgeons favoured non-absorbable sutures throughout, while one quarter employed absorbable sutures for the peritoneum and then used non-absorbable sutures for muscle, fascia, and skin layers. As in all surgery on infants and small children, wound closure must be meticulous and gentle if wound complications are to be avoided.

3. Postoperative Care

Postoperatively all infants are closely watched for twelve to twenty-four hours, and their intake and output are carefully charted. Within three to six hours following surgery, after the infant has recovered from the anaesthetic, oral feedings are begun. At first these consist of small amounts of water administered frequently, and are gradually increased to increasing amounts of milk formula. By the third day, the infant can usually tolerate a full strength formula. If the infant vomits postoperatively after starting oral feedings, the quantity of feeding must be increased very slowly and occasionally it may be necessary to restart the infant on his pyloric feeding series. Since many of these infants are mal-nourished, adequate vitamin supplements must be provided. In many, supplemental parenteral fluid is required during the first twenty-four hours after surgery. Sixty-three infants in our series received fluid by the intravenous route or by hypodermoclysis postoperatively.

The average stay in hospital for all cases was eleven days. It is interesting to note that in the first fifty cases the average hospital stay was thirteen days in comparison to nine days for the last fifty cases. More recently the infants have been discharged from hospital much earlier, usually on the fourth or fifth day. Early discharge from hospital is important in reducing the expense of hospitalization and in preventing the infants from contracting intercurrent hospital infections.

Postoperative Complications

Thirty-three of the infants had significant vomiting during the postoperative period. In twenty-eight cases this vomiting was mild and of short duration, while in five cases it was quite severe and persisted for several days. Persistent, severe postoperative vomiting may be caused by gastric atony, gastritis, peritonitis, (if there has been a mucosal leak), or incomplete division of the pyloric sphincter. Although in this series of one hundred cases, all surgeons employed the Ramstedt technique, some surgeons, compared to others, had a very low incidence of postoperative vomiting in their cases. It would therefore appear that some of the finer technical details of the operation exert considerable influence on the postoperative course.

Severe wound infections occurred in four cases with minor stitch abscesses in seven other cases, giving a total incidence of wound infection of eleven percent. The responsible organism in most cases was a staphylococcus aureus.

In one instance disruption of the wound occurred. This happened fourteen hours postoperatively in an eight week old infant. The type of incision employed was a right rectus muscle split, but the type of suture material was not recorded. With such an early wound disruption, it appears that this incision was improperly closed. The wound was re-closed at a subsequent operation, and the child went on to make an otherwise uneventful recovery.

In one infant, postoperative convulsions occurred. These were believed due to water intoxication caused by overenthusiastic intravenous water therapy. The child responded to parenteral electrolyte therapy. It is exceedingly important not to overload the small infant with fluid. Intravenous water, and electrolyte solutions should only be administered in amounts calculated to correct deficiencies. A slightly dehydrated infant will tolerate surgery much better than an edematous infant whose pulmonary and cardiovascular systems have been overloaded. In infants with only slight or moderate dehydration, intravenous fluids are only rarely required as in most instances the water and electrolyte loss can be corrected safely and adequately by the preoperative administration of normal saline by hypodermoclysis.

Results

Ninety-nine infants in this series of one hundred cases of pyloric stenosis treated by surgery eventually did well, with complete relief from all symptoms. One death occurred in the series. This was a four week old male infant admitted to the hospital on December 13th, 1954. The weight on admission was 2,398 grams. The infant was moderately dehydrated, emaciated, and had the classical physical signs of congenital hypertrophic

pyloric stenosis. The diagnosis was confirmed by x-ray examination of the barium filled stomach. Blood chemistry determinations were performed on the infant at the time of admission, and were all within normal limits. Preoperatively the baby received one hundred cc's of normal saline and two hundred cc's of five percent glucose and water by scalp vein. On December 16th, 1954, a Ramstedt pylormyotomy was performed. No complications occurred during the operative procedure. Postoperatively the child seemed to be doing well without any obvious difficulties. There was no vomiting, no elevation in temperature, and the infant's hydration appeared to be good. The pyloric feeding series was being tolerated well. The infant died suddenly, nineteen hours after the operation without any obvious cause of death. A post mortem examination was performed which showed the pyloric sphincter to be adequately divided. There was no evidence of pulmonary aspiration. The only positive findings were lipoid depletion of the adrenals and generalized body cachexia. Whether or not this infant died of adrenal failure is uncertain.

Summary and Conclusion

In this paper, one hundred consecutive cases of infantile hypertrophic pyloric stenosis treated by surgery at the Winnipeg Children's Hospital have been reviewed. The clinical features, the method of diagnosis, the preoperative care, the operative procedure, the postoperative care, and the results have been described. Only one death occurred in the series.

Acknowledgment

We wish to thank Dr. Colin C. Ferguson for his suggestions and guidance in preparing this paper.

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Bile Peritonitis of Unknown Etiology

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Bile peritonitis of unknown etiology or "perforationless" biliary peritonitis is a rare condition with less than fifty cases reported in the literature. The rarity and interest of this condition warrants the following report:

Case Report

Mr. A. D., a 68 year old white man, was admitted to St. Boniface Hospital at 4.30 p.m. on January 2, 1955. During the previous evening he had consumed a large qualtity of alcohol, estimated at 26 oz. He retired at 3.00 a.m. and arose at 8.00 a.m. feeling reasonably well. About 10.00 a.m., following a light breakfast, he began to suffer a steady, pressing pain over the epigastrium and right upper quadrant of the abdomen The pain gradually became more severe, but remained fairly well localized to this area. During the day he vomited bile stained material on three occasions. His bowels had not moved.

The patient presented himself as a well-preserved male, lying quietly on his back, pale and somewhat shocked in appearance. Oral temperature was 96°F., blood pressure 100/70, pulse 72, regular. Examination of the head, neck and chest was essentially negative. The abdomen was scaphoid, did not move with respiration and exhibited a board-like rigidity. Tenderness to palpation was diffuse, somewhat more localized in the right upper quadrant. Hernial orifices were clear and rectal examination was not helpful. There was no diminution of liver dulness. The peripheral pulses were present and the reflexes were physiological.

It is noteworthy that the patient had been suffering intermittent attacks of pain in the epigastrium and right upper quadrant since January, 1954. During March the pain became more intense, and he was admitted to hospital for investigation. At that time barium series and enema were reported as negative, and an electrocardiogram was interpreted as normal. A gallbladder visualization was not done. In the interval between admissions, the patient continued to suffer pain intermittently, but his activities were not limited.

The immediate laboratory investigation revealed: Hemoglobin—95%, 14.5 gms., WCB—11,300 with a "shift to the left". Serum amylase 100 Somogyi units; Urinalysis was negative. A chest film and a film of the abdomen for free air were both negative.

Despite the absence of free air radiologically, a diagnosis of perforated peptic ulcer was made. At 8.00 p.m. a laparotomy was performed.

The abdomen was explored through a right paramedian incision, and, upon opening the peritoneum, was found to contain approximately 1000 cc of bile, otherwise abdominal exploration was absolutely negative. The lesser sac was opened and the posterior aspect of the stomach and first inch of the duodenum visualized, and nothing noted. Following this the second part of the

duodenum was mobilized, but no perforation was visualized. The gallbladder, except for a few fine adhesions to the colon, was essentially normal. The cystic and common bile ducts were exposed and found to be normal, and no site of leakage could be determined. Morison's pouch was then drained with a penrose drain through a stab wound in the right flank, and the abdomen closed in layers.

The post-operative course was uneventful. A moderate amount of bile drained for the first few days. The drain was gradually shortened and removed on the sixth post-operative day. During convalescence a few further investigations were performed. The peritoneal fluid recovered at operation was positive for bile and contained amylase in the concentration of 500 Wohlgemuth units. It was alkaline with pH of 8 and a culture revealed no growth. Liver function tests were normal and a cholecystogram revealed a normally functioning gallbladder. The patient was discharged on January 13, 1955, feeling well.

On January 27, 1955, the patient presented himself at the Out-Patient Department complaining of right anterior chest pain of three days duration. A chest x-ray demonstrated a small right-sided pleural effusion. No treatment was prescribed and on a further visit February 8, 1955, the patient's symptoms had disappeared and a chest x-ray demonstrated clearing of the fluid. Since that time there have been no further visits to the Out-Patient Department, but correspondence with the patient in August, 1955, found him to be in fairly good health and able to carry out light farm duties.

Discussion

This condition was first recorded in the English literature in 1873 by Saunders.[1] Subsequently there followed reports by Fryer, Barlow, Bargellini and Richardson (1905). However, not until Clairmont and von Haberer[2] published their case and their observations of dog experiments in 1911 was much interest evinced in this entity. There soon followed a host of experimental work and theories as to the causation of perforationless bile peritonitis.

Clairmont and von Haberer[2] thought that this condition was due to filtration of bile through the wall of the gallbladder or the bile ducts (biliary dew). Schivelbein[2] said the filtration was via the glands of Luschka. Wolff[2] ascribed it to leakage from the bile canalieuli from the gallbladder bed. Burchardt[2] (1923) disputed the filtration theory and claimed that bile was loosed through an opening in the biliary tree which subsequently closed over. Cope[2] thinks similarly. In more recent years Pohlman[3] stated that experimental work does not establish the existence of true biliary petitonitis in man without demonstrable perforation, although the perforation may be difficult to find. McLaughlin[4] mentions a microscopic perforation somewhere in the biliary tree. Schlaepfer[5] says ruptured subserous bile ducts on the liver surface, secondary to chronic cholangitis with perforation resulting from sudden increase in intra-abdominal pressure is the cause. Blad[6] claimed the cause to be necrosis of the biliary tree by refluxed pancreatic juice in conjunction with obstruction of the papilla of Vater and increased pressures in the biliary ducts and gallbladder.

As obtains with most conditions that have numerous theories of etiology we merely admit our ignorance of the true cause. Most authors, however, subscribe to the views of Burchardt, Cope, Pohlman.

Regarding the case presented above perhaps one might theorize that the excess imbibition of alcohol the previous night caused an increase of activated pancreatic juice which was refluxed up the biliary tree with subsequent necrosis and minute perforation of the ducts or gallbladder or of a subhepatic biliary canal, and resultant extravasation of a large amount of sterile bile. This theory (Blad) holds most favor especially in view of the amylase concentration of the aspirated bile. Unfortunately, the chloride content of the bile was not estimated to see if H Cl was mixed therein which could presuppose a tiny perforation of the duodenum that had subsequently closed, despite the absence of free air being encountered on opening the peritoneal cavity and despite a pH8 of the examined bile. (This latter supposition has not been encountered in our review of the literature, nor can we substantiate it in any manner. Nevertheless, it is submitted as another cause of the condition).

In retrospect perhaps this patient's previous attacks of abdominal pain were due to minor leakages of bile or to functional dyskinesia of the ampulla of Vater, the latter perhaps being the initiating factor in his catastrophic episode along with alcohol.

Of dubious distinction regarding this case is that it is the earliest one operated upon on record —within ten hours. Most of the cases reported were seen late, at least three days after the onset of symptoms, some even being jaundiced. In only one case was this condition considered pre-operatively.

Summary

1. A case of perforationless bile peritonitis is recorded.
2. Some of the theories of etiology are mentioned.
3. The pathogenesis in our case is described and another possible cause is presented.

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"Problems of the Newborn Infant"

A series of case reports and commentaries from the files of the Winnipeg General, St. Boniface and Children's Hospitals, illustrating factors which affect the survival of the infant during his first week of life.

SERIES XI

Pulmonary Haemorrhage in the Newborn Infant

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and
Georgina R. Hogg, B.Sc., M.D.

Tardieu (1855) first described petechial haemorrhages in lungs and other structures associated with asphyxia.

Since that time there has been considerable interest in pulmonary haemorrhages which occur in the lungs of newborn infants. The haemorrhages may be divided into:

1. Interstitial.
2. Intra-alveolar.
3. Subpleural.

These three conditions usually occur in combination.

One of the main reasons why interest has been roused regarding intra-alveolar haemorrhage is the fact that some workers have suggested that this is a definite clinical entity. While this may be going too far, it is nevertheless one of the manifestations of respiratory distress in the early neonatal period.

In 1923, F. J. Browne suggested that intrapulmonary haemorrhage was a distinct entity and he recorded 3 cases in which the child was well for several days and then had a sudden epistaxis, blanching of the skin, and a sudden rush of blood from the mouth prior to death.

Other workers notably Labate and Grulee confirm what Browne has said, and Labate (1947) states that pulmonary haemorrhage made up 10% of his neonatal mortality.

The following is the case history of a child who died from pulmonary haemorrhage:

Baby H

Male. Mother — P.1, G.4; history of two previous miscarriages. Her previous health was normal and the present pregnancy apparently uneventful until spontaneous onset of labour at 29th week. Labour lasted 2 hours, 16 minutes. The infant was delivered by a Footling breech. No difficulty was experienced with the delivery. The infant was immature and weighed 1,195 grams, his color was good and he had a fair cry. Resuscitation was not necessary. There was a certain amount of intercostal indrawing.

The infant remained well and of good color until 24 hours after delivery, when quite suddenly blood began to pour from his mouth and nose. Intubation was performed, and blood was seen to be welling up from the larynx and trachea. Death occurred shortly afterwards.

We have studied 15 cases of pulmonary haemorrhage and only four had so definite a history as this case. However, 10 out of our 15 infants did present with symptoms of respiratory distress. The 15 cases that were studied all died and from the autopsy material we have classified them as follows:

1. Moderate haemorrhage—involving more than one third of the lung — 9 cases.
2. Severe haemorrhage—involving almost all of both lungs — 6 cases.

Further data in relationship to the pregnancy, etc. were compared with the series of 15 other neonatal deaths of similar birth weight but not suffering from pulmonary haemorrhage. Apart from the fact that in 10 of the cases who died from pulmonary haemorrhage there was evidence of respiratory distress while there were only 4 cases of respiratory distress in the "controls," no remarkable difference was found either in the pregnancy histories, the sex distribution, the labour or delivery.

Microscopic examination confirmed that the bleeding in these infants came from their own lungs and was not aspirated maternal blood. In most cases it was so massive that it could only have been a terminal event. There was no evidence of hemolysis as would be expected in aspirated blood. The origin of the bleeding has been investigated by other workers, notably those in Detroit, who have confirmed that the bleeding in these cases came from the child.

The site of bleeding has been subject to some considerable debate. Avenheim and his co-workers have claimed that the rupture occurs due to inadequacy of elastic tissue in the small veins, and he has brought forward considerable microscopic evidence and experimental evidence to support his views. In the present series of cases studied there was no evidence that the veins in the cases who died from pulmonary hemorrhage were in any way different in the amount of elastic tissue they contained as compared with the "controls." We were unable to find any specific weakness in the vessel wall structure, as has been suggested by Avenheim and his workers.

Three conditions were found to be associated with pulmonary haemorrhage.

From the Department of Pediatrics and Pathology of the University of Manitoba, and the Winnipeg General Hospital.

1. Atelectasis was present in 11 cases, being marked in 6 and moderate in 5.
2. A hyaline-like membrane was present in 8 cases, being severe in 4 and moderate in 4.
3. Plugging of the alveolar ductus was noted in 4 cases.

In the "control" series studied, atelectasis was present in two cases, hyaline membrane was present in three cases and plugging was present in one case.

Because of the engorgement of the lungs with blood, the possibility that pulmonary haemorrhage in the newborn infant was due to a cardiovascular upset and heart failure was considered, and a careful study and review of organ weights was made.

In the weight range 1250-1750 grams there were eight cases who died with pulmonary haemorrhage. In four of these the amount of bleeding was classified as severe and three of these severe cases had lungs which were heavier than the average weight. However, the liver in the same cases showed no increase in weight. The hearts were also of normal size and weight. This does not exclude the possibility that such haemorrhage could have been caused by an acute left ventricular failure. However, we have not seen pulmonary haemorrhage in cases of congenital cardiovascular disease in which failure was thought to have occurred.

A study to determine the presence of infections in such cases was made, and no evidence of inflammatory disease was found in any of the cases which died, and the lung cultures were negative.

Many theories as to the cause of pulmonary haemorrhage have been suggested. Infection has been suggested by some workers, notably Labate. We have, however, found no evidence of pulmonary infection on microscopic examination, nor any positive evidence from attempts at bacterial culture. These findings are in agreement with Browne and Avenheim.

Intracranial haemorrhage has been suggested as a cause in six of our cases, all of whom were very premature, and had some degree of intraventricular hemorrhage, but in these cases, we felt, that it was no more than we see in cases that are extremely premature and suffer from anoxia.

Haemorrhagic disease could well be a possible cause. However, it is surprising, if this is so, that there are no other areas of bleeding or haemorrhage to be found other than in the ventricles, despite a careful search at postmortem.

Although it has been claimed that contraction of the uterus with an excessive rush of blood into the fetal circulation could be a cause of pulmonary haemorrhage, dog experiments do not confirm this, and such transfusion experiments done in newborn pups do not result in pulmonary haemorrhage.

Erythroblastosis is a specific condition in which there is a marked production and destruction of red cells and many of these infants show widespread haemorrhages. Three of our cases suffered from Erythroblastosis.

Anoxia

This appears from our series to be the one single common factor, and it can result from both intrauterine causes and from neonatal factors. Labate suggested that in a breech the close apposition of the mouth to the vagina combined with the respiratory efforts of the foetus could build up such a negative intrathoracic pressure that rupture of the vessels could occur. However, nine of our cases were delivered as a vertex, three as a breech and three by cesarean section, so that this cause, although it may play a part, cannot be the only factor. However lung movements must play a part since apart from intraventricular haemorrhages of small amounts the lungs are the only organ showing massive bleeding.

There is little doubt that hyaline membrane and pulmonary haemorrhage are closely associated. This opinion is shared by Claireux. Further we have noted above, the plugging of the alveolar ducts, and such a state would produce anoxia while at the same time there would likely be violent respiratory movements as a result of the respiratory obstruction. Ten of our cases had clinical respiratory distress. The anoxia would increase the tendency to bleed, while the increased pulmonary effort due to the plugging and presence of hyaline membrane could well raise the intra-alveolar negative pressure to a degree where a vessel rupture would occur with a resultant massive intra-alveolar haemorrhage.

Lastly, the close relationship of hyaline membrane, intra-alveolar plugs and intra-alveolar haemorrhage makes one suspect that all these findings are merely signs of apparent factor and not separate entities, and that, possibly, pulmonary haemorrhage is a late or extreme manifestation of the hyaline membrane syndrome.

Summary

Pulmonary haemorrhage is a finding, not a disease entity. The types of pulmonary haemorrhage are discussed.

The condition presents a clinical picture of respiratory distress in newborn.

The bleeding is from the infant and is associated with atelectasis, hyaline membrane and plugs.

Some suggestions as to the theory as to the causation of this condition are advanced, the commonest single factor present is anoxia.

Medical History

"1855"

Part III

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In Parts I and II it was suggested that though modern medicine began its development with the revival of learning about 1550, nothing of practical importance to sick people at large emerged until about 300 years later, that is, about one hundred years ago. Then, for the first time, treatment and prophylaxis became more effective than it had been since the days of Hippocrates. Various factors involved in the production of modern medicine have been dealt with. In this final part of the subject I shall examine some of the medical literature of one hundred years ago, and contrast the practices and opinions of that day with our own. The material used here will be selected for diversion rather than edification, and it by no means gives a complete picture of the important medical activities of 1855.

Smoking

We find that the tobacco controversy is perennial. In "Practical Observations on the Use and Abuse of Tobacco", John Lizars of the Royal Infirmary, Edinburgh (1857) reflects a common modern attitude. Among other thangs, he says: "The frequency of cancer of the tongue cannot bear any very alarming proportion to the number of persons who indulge in the Virginian weed . . .. nor does insanity bear any ratio to the extent to which smoking prevails". He appeals for a less vituperative and more scientific discussion of the tobacco question and freely admits the possibility of harmful side effects. The battle over tobacco, of course, had gone on since its first introduction to England during the reign of Elizabeth I. By the time of her death (1603) the habit was very general, and tobacco had already become one of the most important articles of import from the American Colonies. During the plague it was regarded as a protective, and even women and children were given instructions in the method of its use. It was also used in enemas and as a cure in erysipelas, syphilis, cancerous growths, etc. Soon afterwards the habit was violently attacked, very largely on moral and hygienic grounds. James I, who is remembered as one of the Scottish literary figures of his day, wrote a diatribe against it ("A Counterblaste Against Tobacco") about 1610. In 1624 Pope Urban VIII published a decree of excommunication against snuff takers, and Innocent XII extend ed it to smokers in 1690. One can imagine that no smoking would be tolerated in Court or Church circles at that time. The objections were not advanced on the grounds of health; for some reason all the Churchmen seemed to feel that there was something immoral about it. Most of us can recall the days when no Minister ever smoked (in the open).

By the middle of the Eighteenth Century it was generally considered vulgar, and resorted to only by the "lower orders". Trevelyan in "English Social History" (1942) says: "The Crimean War (1854) had also its effects in lesser matters. In imitation of our heroes in the trenches before Sebastopol, smoking became fashionable again after being banished from polite circles for eighty years. For the same reason beards returned after an absence of two centuries from well-bred society. The typical mid-Victorian of all classes was a man with a beard and a pipe". It was at this time that cigarettes first became popular in England, and also the well known but anonymous "Ode to Tobacco" was written:

"How they who use fusees
All grow by slow degrees
Brainless as chimpanzees,
Slothful as lizards.
Go mad and beat their wives,
Plunge (after reckless lives)
Razors and carving knives
Into their gizzards."

Syphilization

The success that had resulted from vaccination for smallpox opened the door for speculation and hope in other diseases. Syphilis was still rampant in all civilised countries, and the hospitals were filled with its gross and disgusting lesions. Mercury and potassium iodide were generally known to be only partially successful and had undesirable side effects; so much so that the symptoms of syphilis and mercurial poisoning became difficult to differentiate. It was natural that vaccination should have been thought of. In about 1850 Auzias Turenne advocated vaccination for prophylaxis and for treatment in all stages of the infection. The method consisted of producing a multitude of primary sores over the abdomen, arms and legs by direct inoculation of syphilitic pus; several such punctures were made every week until, in some cases, a series of three or four hundred were created in the course of months. This bold young French experimenter presented his theories and some of his results before the French Acadamy of Medicine. This produced acrimonious debate, mostly having to do with moral implications. Righteous indignation was aroused by the suggestion that the wages of sin should in any way be ameliorated by the interference of medical men. Besides, doubt was cast on the therapeutic

effects. The practice seems to have died out except in the Norse countries; Boeck of Christiania showed particular enthusiasm. His name is preserved in connection with Sarcoid, and he was a first class clinician and pathologist. He did not use syphilisation as a prophylactic nor in primary syphilis, but produced several publications (1854 and 1856) purported to prove its usefulness in "constitutional" syphilis. Some of his case reports are quite convincing. However, the practice seems to have been discarded by 1865, after much altercation in all civilised countries.

"Experimental" Medicine and Psysiology

This was indeed the great age of "experimental medicine"—a term introduced some years earlier by Magendie; the years 1854-55 saw the publication of twenty-five lectures by his successor, Claude Bernard, dealing particularly with the liver and sugar metabolism. This work formed the foundation upon which all subsequent investigation of diabetes was built and really was the beginning of clinical bio-chemistry. Prominence is given to the work of Bernard and his associates in all the publications of the period.

Much attention is given to Ludwig's "Lehrbuch der Physiologie des Menschen", Leipsig 1856. One reviewer states: "Day by day it would seem that the theory which attributes every phenomenon of life to a purely vital cause, ignoring entirely the influence and even the existence of physical force in the manifestation of life, is becoming less and less secure."

Infectious Fevers

We see the profession still vacillating between the ancient idea of telluric causes and contagion. The question of contagiousness of cholera was thoroughly discussed at the American Medical Association in 1855. Much evidence was produced in support of contagion by a report of the disease in St. Louis from 1849-54. It was shown that it made its entrance with immigrants and spread along the lines of communication, which were rivers in those days; this especially applied to routes that had been recently opened. But even up to this time in India, where cholera was ubiquitous and perennial, the doctrine of contagiousness was still repudiated.

To show that the question of contagion had not even then been completely disposed of, we quote from "The British and Foreign Medico-Chirurgical Review" of January 1857. Referring to cholera, they say: "Upon the subject of contagion we do not enter, because its propogation by human intercourse in the manner in which small-pox, scarlatine or measles are propogated, has never been generally believed." Epidemics were found to be referable to two chief heads, "Seasonal or Meteorological conditions" and"Localizing causes". "As regards this country (England) it appears that certain meteorological phenomena which, in the aggregate, borrowing an idea from the older physicians, we term 'pestilential constitution of the year' have mostly accompanied outbreaks of cholera."

The clear clinical differentiation of "typhoid" (continued fever with enteric lesions) and "typhus" fever (cerebral, enteric and sometimes pulmonary lesions) was in most places being made.

As has been pointed out previously, most enlightened practitioners were well aware of the contagiousness of puerperal sepsis. But the idea that it was caused by a living organism and that other infection could be from the same cause was not generally recognized until Pasteur's and Lister's demonstrations in about 1865. In 1856 Sir J. Y. Simpson, of Edinburgh, the most famous obstetrician and gynaecologist of his day, published an article attempting to show that post operative sepsis was essentially the same as post partum sepsis. This produced much discussion, but was not generally accepted. The critics had all varieties of explanation for sepsis after operation, such as "retrograde metabolism", "atmospheric conditions", "pernicious anatomic grouping", "noxious effects of dead or injured tissues" and a dozen other fanciful ideas. The profession was still under the thrall of mysterious vital influences arising de novo. The idea that infections could be transmitted by microscopic organism was really not generally accepted until Koch's demonstrations with anthrax in 1876 and with tuberculosis in 1882.

Surgery

The introduction of general anaesthesia (1846) had greatly enlarged the field of operative surgery. However, it was still 30 years before asepsis was efficiently used, and also haemostasis must have been inadequate. The death rate from major surgery was therefore still appalling.

In "Medical Examiner" of Philadelphia in December 1856, George H. Lyman reviews the statistics on three hundred cases of ovariotomy done by several first class surgeons. Apparently the operation had been under criticism, but the author protests and says: "The mortality attending upon ovariotomy is not greater than it is after other capital operations". These are the figures:

Rate of mortality in all the cases was 40%.
In the 70% in whom the operation was completed, the rate was 43%.
In the unfinished operations the rate was 31%.
Of the fatal cases, 42% were from peritonitis and 25% from hemorrhage.

All other operations involving opening of body cavities carried a similar hazard. Operations on bone were particularly fatal. The one case of removal of a foreign body from a knee joint that I have encountered ended in death. Even lithotrity carried a mortality of 13%; lithotomy was fatal in about 20% of cases.

The abdomen was rarely opened except for ovarian tumors whose size made existence precarious. The first gall-bladder operation was not done until 1867. It was not until 1886 that Fitz (Professor of Medicine at Harvard) began to make the clinical diagnosis of "'appendicitis" and to differentiate it from what has previously been considered to be a disease in and about the caecum, and called "perityphlitis". He recognised its relation to abscess formation and general peritonitis and he began to suggest early operation which had, however, been suggested by several other observers some years earlier. "Early operation" at that time always meant after perforation or peritonitis. Charles McBurney (1846-1913) must be given the credit for having advocated and performed appendectomy before perforation. His first paper on early operation appeared in 1889. Since then, millions of appendices have been removed on the evidence of McBurney's cardinal sign: "A tender point determined by the presence of one finger, very exactly between an inch and a half and two inches from the anterior spinous process of the ileum on a straight line drawn from that process to the umbilicus". It was, of course, the introduction of asepsis and antiseptics that made this and many other sugical operations relatively safe.

Public Health and Sanitation

In England, after the adoption of the Public Health Act in 1848, much attention was given to prevention of disease. Health officers were appointed by various districts and towns. They made an effort to estimate the trend of disease from year to year, but this was very difficult because of the absence of accurate population figures. They paid particular attention to contamination and adulteration of food destitution, over-crowding, water supply, ventilation, adequacy of diet, conditions of employment, disposal of sewage and drainage. The extent to which these activities improved general living conditions and decreased mortality is impossible to estimate from the literature of the period. Many of the Health Officers were not medically trained, and still believed in spontaneous generation of disease and in the malign influence of the "miasma" arising from stagnant water. The reports from various parts of the country were consequently not comparable and no account or comprehensive idea of the health of the country could be formed in spite of the general enthusiasm that was apparent. It was this unsatisfactory condition which produced one more reason for the beginning of state medicine in England. A. W. Barclay in 1856 says: "Since then, the welfare of the general community is so intimately allied with sanitary investigations, the question arises, whether it be possible for single inquirers to cultivate so extensive a field; whether investigations so necessary for the common weal ought not rather to be undertaken by the State; and whether, whilst on the details of local inquiry may be best worked out by local authorities and their officers, the philosophical generalization of the gross materials thereby collected would not be better done under the direction of some superior superintending authority. We incline to this opinion, and think that just as the registration of births, marriages, and deaths; the superintendence of local pauper relief and expenditure; the inspection of factories and the custody of lunatics; are placed under the administration of public boards, so ought all inquiries into the influence of locality, circumstance, and occupation over the health and mortality of the public, to be directed and superintended by the General Board of Health."

Materia Medica and Therapeutics

Up to one hundred years ago the administration of drugs and depletion were almost the only methods of treatment. Almost everyone had his favorite theories, and even lay people often grew medicinal plants of various sorts. The apothecaries were much to the fore; they sometimes actually consulted at the bed side and in spite of the protests of the medical profession, they frequently treated patients without consultation. A time honoured custom that was disappearing in 1855 was consultation between the doctor and the apothecary in the neighbouring "coffee house" which served more than coffee!

The nineteenth century saw much advance in inorganic chemistry. Many new elements and compounds were discovered, nearly all of them were tried therapeutically, and many were credited with medicinal powers. Even oxygen was at first thought to have striking effect on a great variety of complaints, and an institution was actually established for its administration.

The results of the first attempt to use gases medicinally were published in 1794 by Beddoes. During the previous quarter of a century, oxygen, hydrogen, nitrogen and carbon dioxide had been discovered. Beddoes had a good medical education and later spent five years lecturing in chemistry at Oxford. He then went into practice at Bristol. He always had a deep interest in the possible effects of the new gases on animal life and especially on sick people. He did much experimenting on animals, his friends, himself and his patients. James Watt, the famous physicist, collaborated with him in setting up his apparatus. He finally came to believe that inhalation of oxygen would help scrofulous disease and that white swelling was sometimes cured; chronic ulcers healed better than on other treatment, and the gas was beneficial in chlorosis, hypochondriasis, melancholia, cephalalgia, some forms of dropsy, dyspepsia, asthma and leprosy. So enthusiastic did

he become that he founded, by popular subscription, "The Pneumatic Institute" at Bristol. He had no less a person than Sir Humphrey Davey as a director and in charge of the apparatus. The Institute was an immediate success. Patients flocked in with all sorts of diseases and went away loud in the praise of pneumo-therapy; all the distinguished scientists visited the institute. There were air-tight rooms for administering the gases, but most of it was inhaled from oil silk bags. Beddoes thought he had discovered a panacea, as did most of his patients. The bubble exploded accidentally. One day Davey had just finished the preparation of a patient. This preparation consisted of recording the temperature and respirations on a rather complicated contraption. The patient, thinking he had had his treatment, immediately volunteered the information that he felt much better. Davey repeated the performance without giving any gas twice a day for several days until the patient declared himself quite well. Davey then confessed to Beddoes that no gas had been used to effect this striking cure. Beddoes must have been broken-hearted, for he had great faith in his gases. Davey from then on gave up the idea of a profession so unstable as medicine, and confined his energies to chemistry, and of course became famous in that sphere. Beddoes soon gave up the Pneumatic Institute and went in for public health activities. I cite this example to show how readily even highly educated and scientific men can be deceived with regard to the effects of treatment.

The medical profession is frequently criticised because they are stubborn about accepting new treatments without trial. However, the records will show that we have more often been more credulous than critical. Hippocrates says: "And surely it is much to be desired that men would learn a lesson from the Past and not allow every new page in the history of society and of the profession to furnish a repetition of the oft-told tale of supine credulity on the one side, and of audacious folly on the other".

One could write a large volume entitled "Up the Garden Path", recounting the multitude of errors that we have been led into by wishful thinking and prejudiced observation.

There were really no specifics for any disease and hundreds of drugs were used in what we would call a haphazard way. Implicit faith was still placed in complex mixtures, some of which contained as many as a hundred ingredients. Many physicians still cultivated their own herb gardens and mixed their own drugs, some of which were secret. Hundreds of drugs were given, with confidence, which we now know to be inert or harmful.

In the literature of the day we see claims for a multitude of drugs because several patients improved while taking them. For example, glycerine—given in tea or coffee in two or three dram doses,—was highly recommended as a "nutrient" and "alternative" in people who were "more or less anaemic, emaciated and feeble". Cod liver oil and other fish oils had been used in folk medicine for many hundred years. It was used particularly in "scrofula", "struma", "phthisis" and all rheumatic affections. It was not until 1824 that it was regarded to have a specific effect on rickets, and, of course, this was not proved until our own day (after the advent of roentgenology).

Quinine was the only known specific, and as "Peruvian bark" had been known to influence the course of malaria since its introduction into Spain in 1638 by the Countess of Cinchona. But since, in the age we are speaking of, it was impossible to differentiate the various causes of fever with any accuracy, "The Bark" or its alkaloid quinine (isolated in 1828) was administered to almost every one who had the external evidence of fever. Since the clinical thermometer and pulse timing devices were in their infancy, the usual variations in temperature and pulses were in the process of investigation.

Colchicum (Meadow Saffron) had been used for various forms of rheumatism since the days of Dioscorides (40-90 A.D.) but from time to time had been condemned because of its toxic effects. The literature of one hundred years ago is mostly occupied by accounts of its toxic effects, and it was not until comparatively recent years that its products have been used with any degree of confidence.

Soon after syphilis became rampant in Europe (about 1500) various preparations of mercury had been used for its treatment. Until the introduction of arsenicals by Ehrlich (1905) practice varied over a wide range; some practitioners gave large doses of mercury to the point of intoxication (salivation, gingivitis and even loss of teeth) while some others condemned its use. Mercurial inunctions for certain skin disease (possibly syphilitic) had been in vogue by Arabian physicians as early as 1000 A.D. Calomel, until recent years, was a favorite purgative among many practitioners. Also it was alleged to have a salutory effect on the liver, the "sluggish" activity of which was supposed to account for a multitude of vague complaints. Many can still remember the routine practice of giving three to eight grains of calomel as a prelude to the treatment of all acute diseases. This was supposed to dispose of noxious subtances from the bowel and liver. This alleged action has never been well authenticated, and in modern practice the only surviving use of mercury is as a diuretic (Salyrgan, etc.) given parenterally.

Iodine was isolated from seaweed in 1821 and soon after the tincture of iodine and potassium iodine came into great popularity. Potassium

iodine was supposed to help to dissolve fibrous tissue and so was given to many chronic diseases. At one time a solution of potassium iodide was always kept at the bedside of everyone who had "tertiary" syphilis, and he was encouraged to drink as much as he could stomach. The tincture of iodine was widely used as an antiseptic 100 years ago. Many wounds were washed with it, and it was painted on the skin in preparation for all operations. It was also given by mouth sometimes in the hope of sterilising and curing peptic ulceration. Iodoform also enjoyed an equal reputation as an antiseptic and every hospital reeked of it.

Strychnine was discovered in 1818 and one hundred years ago was widely used as a "bitters" to stimulate appetite and also in many chronic debilitating diseases—especially the anaemias. Its actual effect in various conditions is complex and of doubtful benefit. Most of the references of 100 years ago have to do with the recognition and treatment of its toxic effects.

Digitalis leaves (foxglove) prepared in various ways had been a part of folk medicine for some centuries. Withering (1741-1799) got his first intimation of its value from an old woman's secret formula. He published his results on its effect as a diuretic in 1785. Since then it has been used in all sorts of heart disease or oedema from any cause. Its particular effect on fibrillation was only discovered in the present century. Of course, in 1855, its value was much exaggerated; it was for a time highly recommended to excite uterine contraction during bleeding or pregnancy, and at one time it was administered to every case of pneumonia to ward off heart failure; it was also claimed by some to be of benefit in any other sort of inflammatory disease.

In general, the period about 1855 saw the decline in the use of mystical drugs—the horn of a unicorn, powdered cuckoo (insufflated for epilepsy), stewed snails, the milk of a young brunette (for tuberculosis), cow dung poultices for the iliac passion (appendicitis), rind "which comes out of Paradise" (for snake bite) and many others even more fantastic or revolting. These were replaced by known chemical compounds which were used with the same abandon as the older "cures". In spite of the many thousand drugs that were given in profusion, we can say that the only substances that had any real effect on the course of disease were: iron in chlorosis, quinine in malaria, mercury in syphilis, and digitalis in some cases of dropsy. Since these conditions could not be accurately diagnosed, the drugs were given in any conditions that had a superficial resemblance to them. Palliative treatment for pain had made headway; the products of the poppy seed had been used for centuries and morphine was isolated in 1804. The hypodermic use of various drugs was described by Kurzak of Vienna in 1856. In 1829 John Abercrombie (an Aberdonian) had described the pathology of peptic ulceration and advised a bland diet and alkalis, which has been but little improved upon to the present day.

Endocrinology

Though internal secretions had not been conceived as being involved in metabolism, the clinical manifestations of two endocrine diseases were described about one hundred years ago. In 1848 Robert Graves (of Dublin) described several cases which showed tachycardia, palpitation, exophthalmos and diffuse enlargement of the thyroid. These he classed under functional disease of the heart, and it is obvious that Graves was not sure whether the primary disorder was in the thyroid gland or the heart. Also it is true that the posthumous publication of Caleb Hillier Parry (1755-1822) described the association of tachycardia and enlargement of the thyroid in several cases. His patients, however, appeared to be heart failure associated with irregular thyroid enlargement of long standing, and were likely not pure "Graves' disease" as we understand it.

It was in 1855 that Thomas Addison (1793-1860) published his article, "On the Constitutional and Local Effects of Disease of the Supra-Renal Capsules". In this he gives an excellent clinical account of the condition which has ever since perpetuated his name, and he definitely associated it with gross disease of the supra-renals whose function at that time was quite unknown.

Possibly the next advance that was made in endocrinology was in 1873 when Sir William Gull (1860-1890) recognised the relation of the cretinoid state to absence or deficiency of the thyroid gland.

Physical Examination

Laennec's method of chest examination which had first been published in 1819 had now come into general use. This revolutionised the ideas on pulmonary disease. Little of importance has been added to Laennec's pulmonary findings up to the present time. The correct interpretation of heart sounds was delayed because Laennec and his immediate followers thought that the first heart sound was due to the contraction of the auricles, and the second to the contraction of the ventricles. About 1831 James Pope (1801-1841) discovered the true source of the heart sounds by listening to the exposed hearts of stunned asses. From that time to the present day there has been much research and controversy about the precise significance of variation in heart sounds, and the adventitious sounds associated with them. The grosser valvular lesions were soon recognised. In 1832 Corrigan in Dublin demonstrated the physical signs of "Inadequacy of the Aortic Valves". The signs of organic lesions in other valves were not so readily assessed.

This arose from the prevalence of insignificant systolic murmur at the apex and pulmonic area. One hundred years ago these were generally considered to mean organic damage, and as a consequence thousands of healthy people were treated for heart disease. The existence of mitral stenosis as a gross autopsy lesion was demonstrated by Morgagni in 1761, but its incontrovertible physical signs were not clearly set out until Sir James McKenzie did so in the early part of the present century.

The general use of the microscope was beginning to have a profound effect on medical ideas. Though it was first discovered in 1609 by Galileo, it could scarcely be called a practical diagnostic instrument until about one hundred years ago. Leukaemia was recognised by Virchow (1821-1901) in 1845 and his concept of cellular pathology was built about microscopic studies; his great work "Cellular Pathology" was published in 1858 and it can truly be said to have revolutionised the study of pathology and of organic medicine.

The ophthalmoscope was invented about 1850 by Herman von Helmbolz (1821-1894) and for the first time physicians were able to visualise living arteries. Also it made possible scientific refraction, and was in fact the chief influence in the production of the specialty of ophthalmology.

Conclusion

The few examples of progress that was being made about the year 1855—selected from a multitude of others—is sufficient to indicate the enormous activity of that time. It was indeed the age at which medicine began to apply itself to the welfare of the community at large; when the first universal efforts to substitute science for empiricism were made. This effort has gathered force through the years, and I feel that the original proposition that medicine has advanced more in the past hundred years than during all the preceding ages has been justified. Previous to this time medicine was satisfied to study palpable physical structure of man—during health and disease. Any distortion of function or structure was, up to that time, attributed to mysterious vital properties in living tissue which was quite outside of the comprehension or the control of man. Now it began to be asked "Are not some of these changes due to chemical and physical changes that we can understand, and possibly alter?" This produced intense microscopic and chemical investigation and stimulated the hope that specific therapeutic and surgical procedures could also alter the course of these morbid changes.

It is a striking fact that, except for the work of Pinel, (who advocated the treatment of the insane by non-restraint), no special thought was given to mental diseases. They are accepted almost completely, as in the Old Testament, to be inevitable visitation of mystical powers (divine or diabolic). For the first time, a critical and quasi scientific attitude has developed in the study of mental aberrations. For the first time man has confronted and studied his own Psyche. Some practical advances have been made but the whole field is still as obscure as body chemistry was in 1855. Perhaps in 2055 the profession will celebrate our day as the beginning of the scientific study of mental disease just as we remember 1855 as the beginning of living chemistry and bacteriology.

Editorial

S. Valsrub, M.D., M.R.C.P. (Lond.), F.R.C.P. (C.), F.A.C.P., Editor

Prophylaxis in Coronary Disease

Preventive Medicine, so eminently successful in fields of communicable, industrial and nutritional diseases, has failed to establish a similar record of triumph in the fields of chronic degenerative disorders, which now rank foremost as causes of mortality and morbidity. Coronary disease, the leading killer on this continent, is an outstanding example of this failure. Until recently it benefited but little from the prophylactic approach.

If the proverbial ounce of prevention is worth a pound of cure, it should be worth tons of palliation. Since the latter is the only kind of treatment that can be offered to the patients with coronary disease, any attempt at prevention, no matter how hesitant or uncertain, looms large and important. Hence, the wide publicity given to the current progress in this direction.

Prophylaxis, as a rule (with some notable exceptions) is based on a knowledge of etiology and pathogenesis. These are not too well known in the case of coronary disease. In fact, until recently coronary atheromatosis, viewed within the context of generalized arteriosclerosis, has been regarded not as a disease, but as an inevitable accompaniment of the process of aging. It took years of research to demonstrate that it is not a natural process, but a disease with characteristic biochemical, epidemiological and etiological features, a disease which may, possibly, be partly reversible and preventable.

The basic concept that currently prevails in the field of coronary atherosclerosis is that the key factor in atherogenesis is a derangement in the cholesterol - lipid - lipoprotein metabolism. This concept is not an assumption a priori, but a conclusion based on considerable evidence that derives from many sources. It is a summit approached from several directions, a point of convergence for the pathologist, biochemist, clinician and statistician. All the roads of research in atherosclerosis seemed to lead to the Rome of lipid metabolism.

The evolution of this concept can be divided, somewhat arbitrarily, into two stages. The first stage was that of almost exclusive pre-occupation with cholesterol. The reports of cholesterol deposits in atheromatous plaques, of high serum cholesterol in many patients with known coronary disease, of high incidence of coronary atheroma in patients with hypercholesterolemia, of atherosclerosis in experimental animals caused by administration of cholesterol—all seemed to point to cholesterol as the chief culprit in atherogenesis, and to suggest a possible way of prophylaxis. Indeed, numerous attempts were made to reduce the levels of blood cholesterol by elimination of the latter from the diet—attempts that were, unfortunately, doomed to failure.

It soon became apparent that the metabolic disturbance underlying atherosclerosis involved a great deal more than mere simple quantitative relationships between levels of cholesterol in the blood, its content in the diet, and its deposition in atheromatous vessels. Gofman and his associates have demonstrated, by ultra centrifugation methods, the preponderance of large molecules of lipoproteins with flotation rates, Sf10-20 and Sf30-100 in patients with coronary disease. Barr and his co-workers, using the process of electrophoresis, have shown that the beta lipoprotein fraction (with a high cholesterol content) is elevated in cases of myocardial infarction. Keys has confirmed the findings of Barr in a similar, but much more extensive, study of patients with coronary disease in U.S.A., Great Britain, Italy, Spain, South and Central America. The emphasis has, thus, shifted from cholesterol to lipid-lipoprotein cholesterol containing complexes — the second stage of the currently popular concept of atherogenesis.

It was only to be expected that these researches in atherogenesis would lead to the search for factors responsible for the deranged metabolism. Diet, hormones, plant sterols, lipotropic substances and other possible factors came under close scrutiny. The results of these investigations are interesting, as well as promising, but the only ones with immediate applicability to prophylaxis are those concerned with diet. Here the significant finding was, that, although the level of the beta lipoprotein fraction in the serum is not altered significantly by the cholesterol content of the diet, it is affected to a marked degree by the total dietary fat content. Keyes and Brock have both independently arrived at the above conclusion on the basis of very extensive studies.

The next step in the study of dietary factors was an investigation of the relationship of dietary fat to coronary atheromatosis and myocardial infarction. P. D. White, A. Keyes, Nomura, Bjork, Brock and others, reporting from various parts of the globe, are in agreement in their conclusions that population groups, subsisting on a diet low in animal fat, have a much lower incidence of myocardial infarction than their more prosperous neighbours, who partake freely of the "fat of the land."

What are the prophylactic implications of these findings? Should the dietary fat content be reduced, and, if so, under what circumstances? These are by no means easy questions to answer. The

evidence for the complicity of animal fat in the causation of myocardial infarction is persuasive, but by no means conclusive. It is statistical evidence, the result of observation rather than comprehension. Prophylaxis based on this type of evidence does not appeal to the scientific mind. Yet, it is not without precedent, and has been known to be successful in many instances in the past. Vaccination against small-pox and administration of lime juice for prevention of scurvy can be cited as successful examples of prophylaxis, based on observation, and practiced long before the causes of these conditions were known. The question is, thus, not so much of evidence, as of practicability. Is it feasible, or even desirable, to impose a restricted and impalatable diet on large masses of people? Few will go so far as recommending the universal application of this measure. The dissatisfaction in Great Britain, Norway, Finland, and other countries, with a low fat diet during the years of rationing, is still too well remembered. Many, however, will favor the adoption of a diet with a fat content not exceeding 30% of the total calories (instead of the usual 40%) by patients with known coronary disease, particularly those with a past history of myocardial infarction. Some will go along with Gofman in recommending fat restriction in people with high flotation indices, whom they regard as likely candidates for coronary thrombosis. Hardly anyone, however, will completely ignore the evidence, even if he may choose to wait for further confirmation before committing himself to definitive treatment.

It should not be assumed from the foregoing remarks that excess of animal fat in the diet is a factor in the causation of myocardial infarction solely due to its atherogenic action. There is a possibility that coronary thrombosis is not as closely related to coronary atheromatosis as is generally thought. Other factors beside atheroma may play a part in the causation of coronary thrombosis. Fullerton (Proc. R. Soc. Med., 48: 669, 1955) suggests on the basis of experimental evidence, that lipemia, which results from ingestion of meals rich in fat, accelerates clotting. Duguid (Lancet i; 891, 1954) has demonstrated that intravascular clotting may sometimes precede fatty degeneration in coronary arteries rather than follow it. Morris (Lancet 1: 69, 1951) has found in his analysis of autopsy records over the past forty years that, despite the increase in myocardial infarction, the incidence of advanced coronary atheroma has actually decreased. These investigators tending, as they do, to divorce coronary atheroma from thrombosis, do not detract from the prophylactic value of low fat diets, albeit they base it not on its effect on atherogenesis, but on intravascular clotting.

The renewed emphasis on the process of intravascular clotting reopens the question of the prophylactic possibilities of anticoagulants. Some authorities advocate its temporary use in threatened infarction, as manifested by increase in severity and frequency of anginal episodes, and its permanent use in patients who have had more than one attack of coronary thrombosis. Others deplore the prophylactic use of anticoagulants on the grounds of difficulties and dangers involved, as well as uncertainty of results. It would seem that each case considered for this type of prophylaxis would have to be judged on its individual merits.

Other aspects of prophylaxis related to the possible sinister role of excessive smoking, physical effort, lack of exercise, emotional stresses of civilized life, have been studied by various observers. The results of these investigations to date have not been too fruitful. Certainly, they do not compare in significance with the results of the studies of dietary factors in the causation of coronary thrombosis.

It is quite apparent from the above brief outline of recent advances in the field of prevention of coronary disease, that we are still a long way from the goal of satisfactory prophylaxis. We cannot talk of control of coronary disease, as we do of diphtheria or smallpox. Yet, we need not be pessimistic as we were but a few years ago, for bridgeheads have been established for future incursions and a possible eventual conquest.

Ed.

Obituary

Alexander Gibson
1883 - 1956

There have been many links between Edinburgh and Manitoba. John Bunn, the first native-born to practise in the Red River Colony, received his early education and medical training in the Athens of the North. One hundred and twenty years ago George Simpson, whose word was law in Rupert's Land, wrote to Alexander Rowand, son of his dearest friend, that if he chose medicine as his profession he was to go to Edinburgh "that being considered the best medical school perhaps in the world at present." Blanchard, Good, Prowse, A. T. Cameron, William Boyd and J. C. B. Grant are names which come to mind of Edinburgh graduates who have practised and taught in this province. But the Edinburgh man who most deeply impressed his personality on Manitoba medicine was our friend Alexander Gibson.

He arrived in Winnipeg on New Year's Eve, 1913, to succeed E. J. Evatt as whole-time Professor of Anatomy. His teaching was interrupted because of active service in India and Egypt in the 1914-1918 War. On his return he entered practice as an orthopaedic surgeon. His exact knowledge of anatomy led him to devise the posterior and almost bloodless approach in operations on the hip joint. This has been so widely adopted in other centres that he became perhaps the best known of Canadian orthopaedic surgeons.

My contacts with him were in the Scientific Club of Winnipeg, the Winnipeg Medical Society and the Manitoba Sanatorium Board. By instinct and training he was particularly at home in the Scientific Club before which he presented ten to twelve communications perfect in content and form. One of these was on color photography in which he was a pioneer. The Winnipeg Medical Society provided an enthralled audience when he discussed the marvellous mechanism of the foot. At an age when most men consider either retirement or lessening of work he took on a new duty as orthopaedic consultant to the Brandon Sanatorium and travelled regularly to operate on its Indian patients. He was never happier than when he discovered and later described to the Winnipeg Medical Society tuberculous infection in the great trochanter of the femur, a rare site. Quite recently in winter he flew with Dr. W. J. Wood to Island Lake to investigate and report on congenital dislocation of the hip in Indian children.

When the Winnipeg Medico-Legal Society was formed he was a charter member and President. An address given before that Society appeared in the April 1956 issue of the Manitoba Medical Review. He took part in the recent Refresher Course put on by the Medical Faculty of the University. At the annual meeting of the Royal College of Physicians and Surgeons of Canada at Winnipeg in October 1954 he was chosen to give the Address in Surgery. His subject was The Vertebral Column and the wealth of his years of study and research was minted into pure gold. Working to the last he died in harness.

Throughout his life he stood for the highest values. He had qualities of mind and heart which made him stand out and yet he was always quiet, courteous and ready to give his services to the humblest in their need. Memories of these things call to one's mind the words of Robert Burns:

"From scenes like these old Scotia's grandeur springs
That makes her loved at home, revered abroad."

—Ross Mitchell.

◆

Tribute paid by Rev. W. G. Maclean, D.D. at the funeral of the late Dr. A. Gibson, on April 2nd, 1956.

It is my sad and responsible duty to say a word in appreciation of the late Dr. Gibson's life and work. During the past twenty-five years he has been well known to me and what I may have to say is said in sincerity and with some considerable knowledge of who and what the man really was. Dr. Gibson was a shy man—shyness takes many forms with all the difficulties which those who are not shy cannot understand; and with a deeply affectionate nature breaking through a natural reserve. To break through this reserve took time but once taken it was well worth while. His mind was richly garrisoned—a delicate scholar—a tireless reader—avid and eager to the very end—catholic, original, constantly making worthwhile discoveries in lonely unvisited spots in literature, far off from the beaten tracks.

Before he permitted anything to show itself in print, he would say "No one has any right to publish unless he has something to say and has done his best to say it aright." He documented, checked and rechecked his publications. There was nothing slovenly about this man and his work. His knowledge of medicine was profound—he could even breathe life into the dry bones of his own subject Orthopaedics. Combined as this knowledge was with uncommon clarity of mind and lucidity of language, it enabled him to make the complicated simple and the chaotic orderly.

The total impression of his personality on me was his dignity, courtesy, modesty and integrity—above all his devotion to his own subject and to the many students who during his lifetime came under his authority.

A young Scot coming to Canada in 1913 he has poured out liberally his rare and precious gifts in favour of Canada. There was never anything aggressively Scottish in his accent, outlook or temperament, yet he was sturdily loyal to earlier objects of his reverence and he forfeited nothing of what he had derived from the influences of his native soil. Happily for him, there was no appendix in small print, with the powers muffled and the man shrunk to a shadow of himself. His is a life lived out and a grave thoroughly earned. Working to the last the blow fell and he was gone—spared the long agony of pain and helplessness through which so many have to reach their hard won goal.

Dr. William Edward Metcalfe

Dr. William Edward Metcalfe died on March 23 at his home in Portage la Prairie. Born almost 93 years ago in St. Thomas, Ontario, he came west with his parents in 1876. It took three days to make the trip from Winnipeg to Portage la Prairie by ox-cart. In 1892 he graduated in medicine and served as an interne in the Winnipeg General Hospital. He returned to Portage la Prairie in 1902 and practised there until 1944 when ill health caused him to retire. His years of active practice were interrupted only when he did post-graduate work at Oxford University.

He was a former medical superintendent of Portage General Hospital and coroner of the district, an elder of the United Church and a school trustee. He is survived by one son.

Book Review

The Exceptional Child Faces Adulthood. Proceedings of the 1955 Spring Conference of the Child Research Clinic of the Woods Schools, Held in New York City, May 6th and 7th.

This conference was sponsored by the Woods Schools in collaboration with Teachers College of Columbia University and the School of Education of City College of N.Y., and included papers by such well known men as Maurice Fouracre, Salvatore DiMichael, Ernest Roselle, Herman Yannet, and James Garrett. The subject of the mentally retarded child attaining adulthood is discussed from many different points of view. The scope of the problem is surprisingly large—as much as three percent of our population is mentally retarded. The majority of these people (slightly less than 80 percent) are mildly retarded, and can be helped to fit into a "normal" way of life. The 15 percent who are moderately retarded will also profit to some extent with understanding and special help. The definition of the responsibilities of an adult (Fouracre) is most interesting: 1. to obtain and hold a job. 2. to develop good interpersonal relationships. 3. to establish and care for a family. 4. to use leisure time wisely. 5. to assume citizenship roles and responsibilities. 6. to pass on the cultural heritage and to develop a philosophy of life which is in keeping with accepted spiritual, ethical and moral standards.

This is recommended reading for all concerned with the subject, particularly in view of the controversy about municipal contributions to the education of the mentally retarded currently raging in Winnipeg. F. J. C.

Social News

Reported by K. Borthwick-Leslie, M.D.

Hi — I'm tired — Have you ever tried looking after the essentials of your Medical Practice? Do, to the best of your ability, what H. R. H. asks—try and rescue the contents of your own basement, re the threatened flood—my routine nightmare was to get back home in Fort Garry some night, some time, and find the contents of the "Deep Freeze" merrily playing tag in about three feet of sewer water, with the two Cockers drowning themselves diving for frozen sausages, etc. The question, how were the poor dogs to know what could be eaten and what had been . . .

On top of such minor nightmares, there was the young son struggling through 3rd year Engineering exams, cooking his own meals, politely telling the telephone, "Sorry, please call Dr. So and So. I haven't heard from my Mother, I think she must have gone to Timbuctoo for a rest, she should be back next week." She had better be, because next week, May 12th, that same son leaves for somewhere in Germany for a four months tour via the R.C.A.F., so Ma had better start a small recce, as to briefs, shirts, socks, etc., preferably clean, I presume? Now that we've gotten ye social editor and troubles out of our system, shall we proceed to much more important news such as:

Congratulations to Dr. H. S. Sharpe, Brandon, Man., the recipient of award of Serving Brother, awarded by the Priory of Canada of the Most Venerable Order of the Hospital of St. John of Jerusalem at an Investiture at Government House, Winnipeg, April 9, 1956 and to Dr. Noel R. Rawson, Neepawa, also the award of Officer Brother. Both honours presented in recognition of services rendered throughout the year to the St. John's Ambulance Brigade.

Thank you, Dr. Sharpe, for your courtesy in notifying me and to both recipients, sincere congratulations. To my old army friend Dr. Rawson —Greetings, Sir.

♦

It was nice to be greeted the other week by Dr. "Bunny" Munro, with last year's familiar "Aloha." Dr. and Mrs. Munro have just returned from their annual Honolulu holiday, and report that the Hula gals are as attractive as ever, and the sunshine more so this year. They renewed acquaintances with Dr. Claude McCrea and family who were holidaying with Dr. and Mrs. Miendle. Haven't had time to really talk to Bunny, but he surely looks healthy, as do Drs. Ida Armstrong and Helen Marlatt safely back from their motor tour south. Oh, well, come David gets back from Germany and those $2.00 bills pile up in the "Holiday Account" may be I can report in November what the rainy season in California is like. Remind me to get a new permanent.

♦

Gleaned from the Alumni News:

(By the way, have you paid your Fee?)

Dr. A. M. Campbell, B.A. '97, M.D.C.M. '04 was elected President of the Manitoba Auxiliary British and Foreign Bible Society at the Annual Meeting in February.

♦

Dr. Andrew Turnbull, M.D. '29 of Vancouver, President of the Canadian Radiologists Association, was honored in Chicago with a fellowship from the American College of Radiologists.

♦

Dr. J. B. R. Cosgrove, M.D. '44, M. Sc. '48 received a $9,500 grant from the Multiple Sclerosis Society of Canada to assist in his research at Montreal Neurological Institute.

♦

Allen Given McPherson, M.D. '51 received his master's degree from the U. of Minnesota in March, 1956.

♦

Gleaned from Dr. P. H. Thorlakson:

(A new grapevine stooge!)

Dr. and Mrs. Thorlakson have just returned from a months holiday in Arizona, having a grand rest. They were entertained by our old friend, ex Bomber Star Dr. Art Stevenson and Mrs. Stevenson. Art is located in Phoenix, Arizona, and is very happy, healthy and prosperous. Also in Phoenix, Arizona, Dr. Gordon Geisler, originally of Winnipeg, then Melville, Sask. (address, 7818 N. 16th) is in General Practice, Surgeon and Dermatologist. Dr. and Mrs. Geisler now have three children, Judith, Duncan and Bradley.

Robert H. Thorlakson just this week is back home after five years of P.G. study in London, England, and the Provinces. He obtained his F.R.C.S. and will be located in Winnipeg.

♦

Did you hear about a certain Irish medico and family, who refused to believe that our dirty little Red River could do anything nastier than be dirty, but really became respectful, when that gal went floating past on an ice floe? The natural interpretation was that all points south had given up the ghost. Poor Pat.

♦

Dr. and Mrs. Sidney Kobrinsky, Kingston Crescent, announce the arrival of Joel David, March 28th.

♦

In Sanford, Man., April 14th, Beverley Rose McNamara of Norfolk, Virginia became the bride of Dr. Ted Cuddy. Dr. Patricia Pickard attended the bride. Dr. Ross Campbell of Brandon was best man. Ushers were Dr. A. Downes and Keith Cuddy.

Dr. and Mrs. Cuddy will reside in Winnipeg.

Dr. and Mrs. A. Moyse, Winnipeg, announce the engagement of Adele Victoria, Montreal, to Mr. W. Cecil Rowe of Calgary, formerly Montreal. The wedding, May 1st in St. John's Cathedral, Winnipeg. Miss Moyse, R.N. is a graduate of the Royal Victoria Hospital, Montreal.

♦

Dr. and Mrs. H. Chochinov of Neepawa, announce the birth of a second son, Ian Clarke.

♦

Dr. and Mrs. Peter Berbrayer happily announce a baby brother for David, on April 9, 1956.

♦

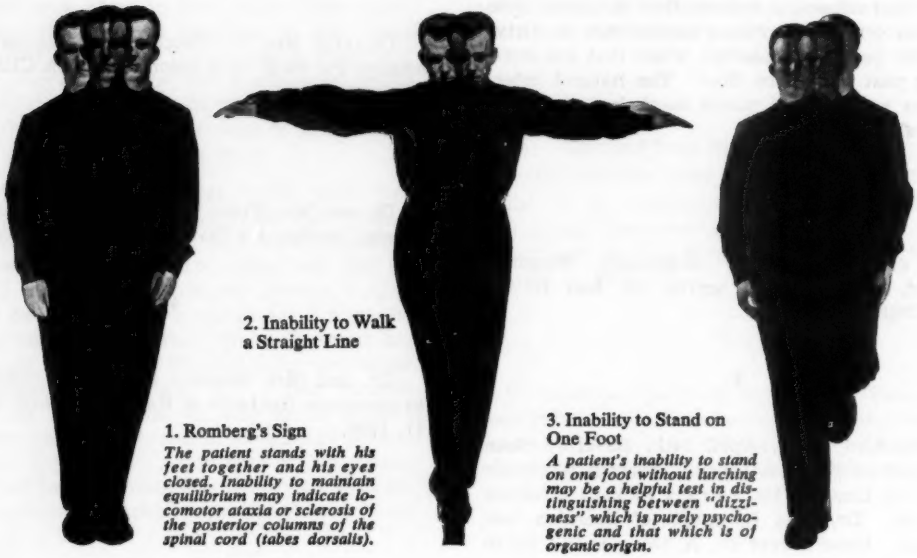
Dr. and Mrs. Stephen Drulak are very happy to announce the birth of Karen Margaret on April 11, 1956.

♦

Dr. and Mrs. C. N. Edwards announce the birth of Daniel Stewart on March 31, 1956.

Notes on the Diagnosis and Management of "Dizziness"

II. False Dizziness



1. Romberg's Sign

The patient stands with his feet together and his eyes closed. Inability to maintain equilibrium may indicate locomotor ataxia or sclerosis of the posterior columns of the spinal cord (tabes dorsalis).

2. Inability to Walk a Straight Line

3. Inability to Stand on One Foot

A patient's inability to stand on one foot without lurching may be a helpful test in distinguishing between "dizziness" which is purely psychogenic and that which is of organic origin.

False dizziness is a sensation of sinking or lightheadedness which is often of psychogenic origin. It should be distinguished from true "dizziness" or vertigo[1] in which there is a definite whirling, moving sensation.

Unsteadiness, lightheadedness and similar manifestations of false dizziness[2] may be psychogenic or the result of arteriosclerosis, hypoglycemia, drug sensitivity and general metabolic disturbances such as anemia and malnutrition. Hypertension is often the cause of these symptoms.

Psychogenic dizziness probably originates at the highest brain centers. It may be described as a sense of uncertainty with occasional mild lurching but not to the point of falling. In these patients there is no nausea, no disturbance of vestibular pathways and otologic and neurologic examinations are negative. The sensation is unaffected by head movement. Symptoms usually disappear[3] with complete rest.

Dramamine® has been found highly effective in many of the conditions already mentioned. Maintenance therapy with Dramamine will often keep the patient from becoming incapacitated by his condition.

Dramamine is also a standard for the management of motion sickness and is useful for relief of nausea and vomiting of fenestration procedures and radiation sickness and for relief of "true dizziness" of other disorders.

Dramamine (brand of dimenhydrinate) is supplied in tablets (50 mg.) and liquid (12.5 mg. in each 4 cc.). G. D. Searle & Co., Research in the Service of Medicine.

1. Swartout, R., III, and Gunther, K.: "Dizziness:" Vertigo and Syncope, GP *8*:35 (Nov.) 1953.

2. DeWeese, D. D.: Symposium: Medical Management of Dizziness. The Importance of Accurate Diagnosis, Tr. Am. Acad. Ophth. *58*:694 (Sept.-Oct.) 1954.

3. Kunkle, E. C.: Central Causes of Vertigo, J. South Carolina M. A. *50*:161 (June) 1954.

Abstracts from the Literature

Atrophic gastritis; a five-year survey of thirty-two cases proven by gastric biopsy. Fairley, K.F., Turner, C.N., Mackay, M.A., and Joske, R.A. M.J. Australia, 2; 1085, (Dec.) 1955.

Thirty-two patients with histologically proved atrophic gastritis were followed for 5 years. There were 12 males and 20 females. Five were asymptomatic. The others complained of recurrent gastric pain and/or flatulence. Some had diffuse epigastric tenderness on deep palpation. No correlation was found between diet or psychic stress and the severity of mucosal change. Twelve patients disliked meat. Twenty-eight patients had barium meals, with 2 negative results. One benign gastric ulcer was noted, one was suspected. A close negative correlation was found between the severity of mucosal change and free acid. Over 5 years, no reduction in acid secretion beyond that first noted was found in 25 patients. Some had more acid on the later tests. Little change was noted in histology between specimens of the gastric mucosa taken 5 years apart. Over 5 years, no patient developed gastric carcinoma. The overall picture of atrophic gastritis was that of a quietly progressive lesion little influenced by therapy and rarely sufficiently disabling to interfere grossly with the patient's mode of life. Atrophic gastritis should be considered in the differential diagnosis of upper abdominal pain and discomfort. Hemorrhage may occur from acute erosions in the chronically inflamed mucosa, and these may heal without development of a chronic gastric ulcer. Therapy at present is inadequate in patients with atrophic gastritis.

Reference
M. J. Australia, 2: 1085, (Dec.) 1955.

Arnold G. Rogers. 3/23/56.

◆

Jaundice Associated with Thorazine (Largactil) simulating Methyltestosterone Jaundice. Kreps, S.I., N.Y. State J. Med., 55: 2957, 1955.

Two cases of jaundice following chlorpromazine are reported. Recovery followed in 4 to 6 weeks after stopping the drug, using general supportive therapy. The liver function studies revealed a pattern similar to that found in patients with Methyltestosterone jaundice. In early stages, there was bile in the urine, the stools were light in color, the bilirubin was moderately elevated, the cephalin flocculation and thymol turbidity tests were normal, as were the total protein and albumin globulin ratio. In both patients the cholesterol esters were reduced, and the free fractions elevated. In one the alkaline phosphatase was markedly elevated. In one it was slightly up. A fall of hemoglobin and red cell concentrations was found in both patients, with no cause but the hepatitis being found in one. The differential diagnosis of jaundice should always include drug-induced jaundice.

Arnold G. Rogers.

◆

Relief of Resistant Edema by Utilization of a "Sump" Phenomenon. Schemm, F.R., and Camara, A.A. Circulation, XI.; 411, 1955.

The authors call attention to a means of bypassing "reluctant' kidneys in order to relieve the resistant massive edema of patients with cardiac or renal disease.

The "Sump" phenomenon is based on the observation that when patients with ascites and peripheral edema, due to heart disease or liver cirrhosis, underwent paracentesis, the peripheral edema often decreased. This was due to free drainage of part of the remaining edema fluid into the peritoneal space from which the aspiration had been made.

Fourteen patients with ascites and/or hydrothorax were treated by seventy-seven aspirations at one to seven day intervals or as soon as fluid re-accumulation was evident. In this manner large quantities of fluid and salt were removed from the body. Plasma proteins and sodium levels were unaffected by the procedure, even after as much as eight litres of fluid were withdrawn at one sitting. (It is the authors' opinion that these complications are noted only in patients with liver cirrhosis). In most of the instances cited, when dry weight was established, it was maintained thereafter by routine medical measures.

This simple procedure of frequently repeated aspirations of ascitic or pleural fluid would seem to be a worth-while measure in many patients with cardiac failure or nephrotic syndrome.

D. H. Stein.

Comprehensive Testing of Gastric Secretory Function. G. B. J. Glass and M. Rich., Amer. J. Gastroent, 24; 137, 1955.

Gastric analysis measuring acid response alone is adequate. Fasting specimens, as well as after histamine stimulation, and after I.V. insulin, were analyzed. Volume, pH, free and total acid, pepsin, glandular mucoprotein, and gastric mucoproteose were measured. Patients with duodenal ulcer showed high values after insulin for acid, pepsin, and mucoprotein, but not after histamine. Gastric ulcer patients, however, do not differ from the controls. Patients with gastric atrophy and macrocytic anemia (especially pernicious anemia) showed extremely low outputs of acid, pepsin, and mucoprotein after histamine and insulin. With gastric carcinoma of the mid portion of the stomach, flat secretory patterns for acid and mucoprotein with insulin are obtained. In gastric atrophy, mucoprotein secretion was impaired, but mucoproteose, from the surface epithelial element, was normal or high (concentrations). The secretion of the vagotomized stomach was normal or almost so after histamine, but negative after insulin.

Dissociated secretory patterns are important. The "positive" pattern has acid and mucoprotein response with insulin hypoglycemia (normal). "Strongly positive" patterns are found in duodenal ulcer. "Negative" patterns, with complete or almost complete absence of acid, pepsin, and mucoprotein to insulin, are found in pernicious anemia, atrophic gastritis, diffuse gastric carcinoma, or bilateral vagotomy. It is due to atrophy of fundal glands or vagotomy. "Dissociated patterns" have low or no acid response to insulin, with normal pepsin and mucoprotein. This was seen characteristically after subtotal gastric resection, with removal of the pyloric part of the stomach.

Patients with diffuse gastric carcinoma usually have no or low mucoproteins with insulin. Normal values suggest the sites of mucoprotein formation, the fundus and body of the stomach are not involved.

Comprehensive test of gastric secretory function after humoral and vagal stimulation is of great importance for evaluation of the functional status of the stomach, and the extent, nature and localization of the underlying anatomical lesion. The methods are suitable for routine clinical use.

A. G. Rogers.

North of 53 District Medical Society

The meeting of the North of 53 District Medical Society was held on Friday, March 2nd at Flin Flon.

Present were: Doctors E. D. R. Bissett, M. K. Brandt, S. L. Carey, C. W. Clark, C. S. Crawford, J. P. Gemmell, P. Johnson, M. T. Macfarland, C. A. Milanese, J. McKenty, J. M. McMahon, H. L. McNichol, E. L. Redpath, W. C. Taylor, R. K. Watson, G. L. Willson.

Following a turkey dinner at the Company Staff House, visitors were conducted through the plant of the Hudson Bay Mining and Smelting Company by Mr. M. A. Roche, Assistant to the General Superintendent.

Afternoon tea was served at the home of Dr. and Mrs. Harvey McNicol and a reception at the home of Dr. and Mrs. Percy Johnson preceded dinner.

The business session was presided over in the absence of the President, Dr. N. Stephansson, by Dr. G. L. Willson; Dr. E. L. Redpath was secretary. Officers were elected for the ensuing year as follows:

President: Dr. S. L. Carey, Clearwater Lake San., The Pas; Secretary-Treasurer: Dr. J. Leicester, The Pas. Rep. to Executive, M.M.A.: Dr. H. L. McNicol, Flin Flon.

Dr. Jack McKenty gave a talk on the organization and work of the College of General Practice.

It was agreed that the next meeting be held at the Sanatorium at The Pas.

A Scientific session was held in the Staff House and consisted of the following: Dr. W. C. Taylor spoke on "Acute Respiratory Diseases in Infants"; "Symposium on Thyroid Diseases" by Doctors J. P. Gemmell and C. W. Clark.

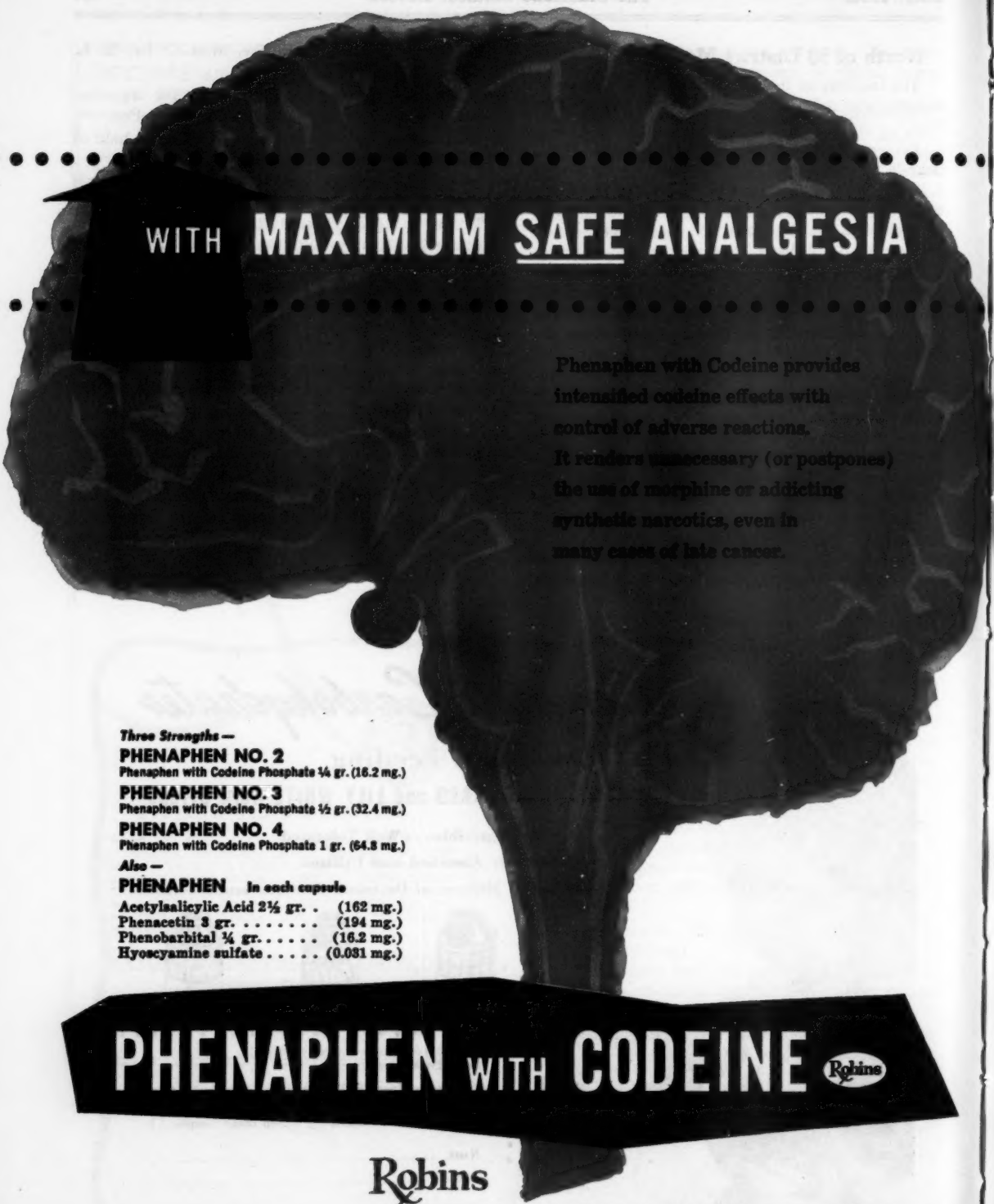
Dr. Macfarland, Executive Secretary, expressed regrets that the President, Dr. Ruvin Lyons, was unable to attend, and discussed matters of importance to the profession including the study of M.M.S. which has been undertaken by an independent Commission under the Chairmanship of Dr. Paul L'Heureux.

Following the meeting members were entertained at the home of Dr. and Mrs. Harvey McNicol.

On Saturday morning, March 3rd, a clinical session including the presentation of cases was held at the General Hospital where lunch was served by the courtesy of the Sister Superior and Staff.

Reported by M. T. Macfarland, M.D.

Raise the Pain Threshold



WITH MAXIMUM SAFE ANALGESIA

Phenaphen with Codeine provides intensified codeine effects with control of adverse reactions. It renders unnecessary (or postpones) the use of morphine or addicting synthetic narcotics, even in many cases of late cancer.

Three Strengths —

PHENAPHEN NO. 2
Phenaphen with Codeine Phosphate ¼ gr. (16.2 mg.)

PHENAPHEN NO. 3
Phenaphen with Codeine Phosphate ½ gr. (32.4 mg.)

PHENAPHEN NO. 4
Phenaphen with Codeine Phosphate 1 gr. (64.8 mg.)

Also —

PHENAPHEN In each capsule

Acetylsalicylic Acid 2½ gr. . (162 mg.)
Phenacetin 3 gr. . . . . (194 mg.)
Phenobarbital ¼ gr. . . . . (16.2 mg.)
Hyoscyamine sulfate . . . . . (0.031 mg.)

PHENAPHEN WITH CODEINE Robins

Robins

A. H. ROBINS CO. OF CANADA, LTD., MONTREAL, QUEBEC

Ethical Pharmaceuticals of Merit since 1878

Department of Health and Public Welfare

Comparisons Communicable Diseases — Manitoba (Whites and Indians)

DISEASES	1956		1955		Total	
	Feb. 26 to Mar. 24,'56	Jan. 29 to Feb. 25,'56	Feb. 27 to Mar. 26,'55	Jan. 30 to Feb. 26,'55	Jan. 1 to Mar. 24, '56	Jan. 1 to Mar. 26,'55
Anterior Poliomyelitis	2	1	1	1	3	2
Chickenpox	86	126	172	203	296	532
Diphtheria	0	0	0	0	0	1
Diarrhoea and Enteritis, under 1 year	9	15	1	6	28	9
Diphtheria Carriers	0	0	0	2	0	2
Dysentery—Amoebic	0	0	0	0	0	0
Dysentery—Bacillary	1	3	1	0	5	2
Erysipelas	2	1	1	2	6	3
Encephalitis	0	0	0	0	0	0
Influenza	9	14	12	2	28	20
Measles	210	256	494	606	604	1351
Measles—German	31	36	27	8	72	39
Meningococcal Meningitis	0	1	2	3	2	7
Mumps	196	171	172	214	479	500
Ophthalmia Neonatorum	0	0	0	1	0	1
Puerperal Fever	0	1	0	0	1	0
Scarlet Fever	21	18	19	30	57	72
Septic Sore Throat	0	4	1	6	4	7
Smallpox	0	0	0	0	0	0
Tetanus	0	0	0	0	0	0
Trachoma	0	0	0	0	0	0
Tuberculosis	48	29	39	31	92	86
Typhoid Fever	0	0	0	0	0	0
Typhoid Paratyphoid	0	0	0	0	1	0
Typhoid Carriers	0	0	0	0	0	0
Undulant Fever	1	1	0	0	2	0
Whooping Cough	28	36	78	92	73	233
Gonorrhoea	123	106	60	93	328	233
Syphilis	8	7	15	19	18	38
Jaundice Infectious	25	33	20	45	70	88

Four-week Period February 26th to March 24th, 1956.

DISEASES (White Cases Only) *Approximate population.	*949,000 Manitoba	*861,000 Saskatchewan	*2,835,000 Ontario	*2,952,000 Minnesota
Anterior Poliomyelitis	2	—	2	4
Chickenpox	86	—	1961	—
Diarrhoea and Enteritis, Under 1 Year	9	21	—	—
Diphtheria	—	—	—	11
Diphtheria Carriers	—	—	—	—
Dysentery—Amoebic	—	—	—	1
Dysentery—Bacillary	1	—	11	5
Encephalitis Infectious	—	—	—	—
Erysipelas	2	—	3	—
Influenza	9	8	163	11
Jaundice, Infectious	25	140	36	66
Measles	210	21	3222	53
German Measles	31	—	1956	—
Meningitis Meningococcus	—	—	7	4
Mumps	196	7	1764	—
Ophthal. Neonat.	—	—	—	—
Puerperal Fever	—	—	—	—
Scarlet Fever	21	4	744	160
Septic Sore Throat	—	5	3	71
Smallpox	—	—	—	—
Tetanus	—	—	—	—
Trachoma	—	—	—	—
Tuberculosis	48	44	90	92
Typhoid Fever	—	3	6	3
Typh. Para-Typhoid	—	—	—	—
Typhoid Carriers	—	—	—	—
Undulant Fever	1	—	1	3
Whooping Cough	28	20	49	13
Gonorrhoea	123	—	—	—
Syphilis	8	—	—	—

DEATHS FROM REPORTABLE DISEASES
March, 1956.

Urban—Cancer, 63; Influenza, 1; Pneumonia Lobar (490), 4; Pneumonia (other forms), 8; Later effects of Poliomyelitis, 1; Tuberculosis, 1. Other deaths under 1 year, 25. Other deaths over 1 year, 211. Stillbirths, 16. Total, 330.

Rural: Cancer, 33; Measles, 3; Pneumonia Lobar (490), 2; Pneumonia (other forms), 11; Syphilis, 1; Tuberculosis, 1; Whooping Cough, 1; Diarrhoea and Enteritis, 1. Other deaths under 1 year, 12. Other deaths over 1 year, 141. Stillbirths, 6. Total, 212.

Indians: Influenza, 1; Measles, 1; Pneumonia (other forms), 2; Whooping Cough, 2. Other deaths under 1 year, 3. Other deaths over 1 year, 9. Stillbirths, 1. Total, 19.

♦

Poliomyelitis—At date of writing (April 10th) only four cases have been reported in Manitoba in 1956. Three of these from the Glenboro area and one from the City of Winnipeg. Three show some paralysis and one has none. Polio virus of the Brunhild (Group 1) type was recovered from the faeces of the Winnipeg case by the Virus Laboratory under Doctor Wilt. This shows the value of laboratory work. Salk Vaccine is being distributed as we receive it.

Chickenpox, Measles and **Mumps** are still quite prevalent.

Gonorrhoea—Shows a definite increase to date this year and Syphilis a decrease. The occasional primary chancre is being found which is rather worrying to control authorities.

A Request for Your Co-operation . . . from the Chairman of the Scientific Program Committee

The Annual Meeting of the Manitoba Medical Association will be held October 15, 16, 17 and 18 in Winnipeg, at the Royal Alexandra Hotel.

In order to insure the success of this important event, the Scientific Program Committee invites the co-operation and assistance of all members of the Association in the planning of the program. Everyone can help by offering constructive criticism and suggestions with regard to the type of papers they would desire to be presented.

The Program Committee also wishes to remind everyone planning to submit papers for presentation at the meeting that the deadline for the mailing of abstracts of papers, is June 15, 1956.

Letters with suggestions, as well as summaries of papers, should be mailed to the Chairman of the Scientific Program Committee, Dr. L. R. Rabson, Mall Medical Building, Memorial Boulevard, at St. Mary Avenue, Winnipeg 1, Man.

Jot Down Your Suggestions . . . . . Mail Them Now!

Children's Hospital
Winnipeg, Man.

Re: Ward Rounds and Clinical Conferences

1. Weekly Grand Round 11 - 12 a.m. Thursday mornings throughout the year.

2. Medical Staff Clinical Luncheon, the first Friday of each month (except July and August), 12.30 to 2 p.m.

3. Special Tuesday noon conferences 12 to 1,
   First Tuesday of the month, Therapeutics, (Dr. Nickerson).
   Second Tuesday, X - ray Diagnosis, (Dr. Childe).
   Third Tuesday, Cardiac Conferences, (Drs. Ferguson, Medovy, Armstrong, etc.).

All these meetings take place in the Playroom at the East end of the first floor.

The members of the Medical profession are invited to attend these Conferences and Ward Rounds.

Physicians' Art Salon

The Physicians' Art Salon Committee invites any Canadian physician or medical undergraduate to enter his work in the 1956 Salon to be held in the Chateau Frontenac, Quebec City, from June 11th to the 15th. This will mark the 12th year for this popular art and photographic feature of the annual C.M.A. Convention. It is sponsored by Frank W. Horner Limited, Montreal.

Conditions of Entry

The Salon structure will remain the same as last year. Entries will be accepted in three sections:

1) Fine Art
2) Monochrome Photography
3) Color Photography

The Fine Art Section is further subdivided into traditional, contemporary (modern), and portrait categories. There is no restriction on media, oil, tempera, gouache, water colour, charcoal, pencil, or dry brush are acceptable in each.

In Monochrome Photography, four entries may be submitted, but each exhibitor is limited to three entries in Fine Art, and Colour Transparencies. And any exhibitor may enter up to the limit in one or more sections.

There is no charge. All costs, including transportation to and from Quebec City will be borne by Frank W. Horner Limited.

Judging of Awards

All acceptable entries will be displayed in the Salon and then judged for awards by a competent jury to be selected by the Art Salon Committee.

To Obtain Entry Forms

Any physician or medical undergraduate interested in submitting work may obtain an entry form with details by writing the sponsor at P.O. Box 959, Montreal. A short note or postcard will do. The entry form contains complete instructions on how to prepare and ship the entries.

Art Salon Calendar

A novel by-product of the Salon, the Physicians' Art Salon Calendar, will be prepared by Frank W. Horner Limited. The Calendar reproduces award-winning work in full colour, and is distributed to all the physicians in Canada, with the compliments of the Company.

Detailmen's Directory

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